Introduction to Practical High Resolution Nuclear Magnetic Resonance Spectroscopy

D. Chapman
and
P. D. Magnus

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Preface

Nuclear magnetic resonance (n.m.r.) spectroscopy has provided organic chemists with an elegant physical method of looking at hydrogen atoms within organic molecules.

Important structural information can be obtained using this technique alone or in combination with other spectroscopic techniques such as ultraviolet, infrared and mass spectroscopy.

No modern organic chemist can work satisfactorily without a working knowledge of the technique.

The purpose of the book is to provide chemists with a concise and convenient source of the elementary theory and also practical information of n.m.r. spectroscopy for everyday use at the working bench.

A short introduction to the basic theory and experimental techniques of n.m.r. spectroscopy is given as well as a number of examples illustrating the application of the technique to structural problems in organic chemistry. A series of recently compiled correlation tables is provided.

It is hoped that this little laboratory manual will provide a useful introduction and source of practical information, in a readily digestible and accessible form, for both student and experienced research worker.

D. Chapman

May 1966

P. D. Magnus

AUG 22 '67

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Foreword

The applications of nuclear magnetic resonance (n.m.r.) spectroscopy to organic chemistry have grown apace since the first spectrum of ethyl alcohol was obtained in 1951. Nowadays every modern chemical laboratory uses n.m.r. spectroscopy as a standard technique. Sometimes the technique is used by itself, especially in unravelling the subtler details of conformation and of conformational interconversions. At other times, it is combined with the older techniques of u.v. and i.r. spectroscopy for following the course of chemical reactions and for structural analysis. The combination of n.m.r. spectroscopy with mass spectral measurements is also a very powerful tool in structural studies. As well as the organic chemist the biochemist is also finding the technique a useful one, both for straightforward structural work and also for probing the delicate and important interactions which take place between biological molecules. The use of relaxation-time studies for exploring these interactions may be expected to grow in the coming years.

There are now available a number of excellent extended texts discussing the principles and theory of n.m.r. spectroscopy. The authors of the present text have set themselves the more modest task of providing a simple introduction to the subject for practical use in the laboratory. They have produced, in fact, an easily intelligible practical laboratory manual. The simple theory of n.m.r. spectroscopy is included in the first part of the book and a whole range of useful correlations, taken from the recent scientific literature, is given in the second part. The book can be warmly recommended to all students and research workers in Organic Chemistry. It will also be valuable in those branches of natural science where the structural aspects of organic molecules are of importance.

D. H. R. Barton

I. THEORY AND TECHNIQUES

1. Introduction

The aim of this book is to provide a short, concise account of the simple theory and practical aspects of high resolution nuclear magnetic resonance spectroscopy. Only the essential theory is included, and the emphasis throughout the book is on the practical uses of both the qualitative and quantitative aspects of this branch of spectroscopy. It is intended primarily for the organic chemist and biochemist, but others interested in this technique should also find it useful.

We discuss first the origin of chemical shifts and spin–spin coupling multiplicity giving examples of the various appearances in the spectra arising from these effects, including AB, AB_2, ABX, A_2B_2 and AB_3 systems. The units used to describe the spectra are defined. Exchange effects and relaxation are also discussed. Longer and more detailed texts of the basic theory of n.m.r. spectroscopy are available elsewhere.[1–3] Other useful sources[4–12] are also given on page 65.

We next discuss the uses of n.m.r. spectroscopy for the determination of molecular structure, the interaction between molecules, including molecules of biochemical interest, the study of reaction kinetics and also more fundamental studies. We discuss some of the various n.m.r. spectrometers available operating at both 60 Mc/s and 100 Mc/s frequencies, pointing out their specific advantages, and provide a list of the specifications of a number of commercial instruments. The use of different solvents and of special sample containers are described and the shifts observed with various solvents discussed. Effects due to hydrogen bonding, hindered rotation and exchange phenomena are also described.

The sources of errors and the limitations on accuracy of the apparatus, and of the technique itself, are pointed out throughout the book as well as the factors determining the quality of the spectra. The precautions required for the optimum use of the instruments are discussed. The use of spin decoupling units for simplifying the interpretation of spectra is illustrated. A number of typical spectra of organic molecules are clearly discussed so as to illustrate the method of interpreting n.m.r. spectra.

An up-to-date list of correlation tables of chemical shift and spin–spin coupling constants for protons, phosphorus and fluorine are included. These are arranged in order of chemical shift values which we consider to be the most suitable for easy reference.

2. Elementary Theory

Some nuclei possess the property of spin and are associated with an angular momentum. The total angular momentum of a nucleus is given by $(h/2\pi)[I(I+1)]$ where h is Planck's constant and I is the spin quantum number which may have values $0, \frac{1}{2}, 1, \frac{3}{2} \ldots$ depending upon the particular nucleus. Those nuclei having a value $I = 0$ do not possess the property of spin. As a spinning charge gives rise to a magnetic moment, those nuclei with a value of I greater than zero also have a magnetic moment μ. If we place a nucleus having a magnetic moment into a magnetic field, it experiences a torque, similar to that which occurs with a compass needle, and, because of its angular spin, this "little bar magnet" precesses at a characteristic frequency around the magnetic field, just as a toy

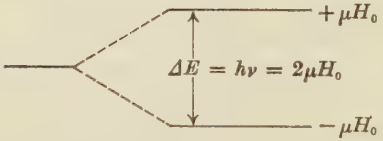


FIG. 1. Energy levels for proton nuclei in magnetic field H_0.

gyroscope precesses around the earth's gravitational field. The potential energy of this nuclear magnet under these conditions depends upon its orientation in the field.

If we consider the behaviour of a molecule containing a proton (^{1}H) when it is placed in a magnetic field (H_0), we know that $I = \frac{1}{2}$ and we see that the proton can lie in the field in a configuration either parallel to the field where it will have potential energy $-\mu H_0$ where μ is the magnetic moment of the proton or is antiparallel with a potential energy μH_0 (Fig. 1). Thus the presence of the magnetic field has created, for the magnetic nucleus, two energy levels which were previously degenerate. Other nuclei having a different value of I give other energy levels of a number equal to $(2I+1)$ The basis of spectroscopy is the Bohr relationship $\Delta E = h\nu$ where ΔE is the energy separation between the energy levels and ν is the radiation frequency. If now the proton is subjected to a radio frequency field such that

$$h\nu = 2\mu H_0 \qquad (1)$$

then it can absorb radiation if it is in the lower energy level, or emit radiation if it is in the upper state. If we have a large number of molecules the protons can distribute themselves among these two energy levels, the ratio of the populations of the levels being determined by the Boltzmann factor $\exp(2\mu H_0/kT)$. If the distribution of nuclei was the same in the upper and lower energy levels of course no net absorption of radiation would occur. At room temperature, however, there are more nuclei in the lower level than in the upper level, although the excess is extremely small and amounts to only some three or four nuclei out of every million. As the transition probability for absorption and emission is equal, there is only a very small net absorption of energy by the nuclei in the magnetic field from the existing electro-magnetic radiation. This means that sensitive electronic circuitry is necessary to detect the resonance absorption. Relaxation effects are important in preventing saturation from taking place.

Hence n.m.r. absorption occurs when certain nuclei are placed in a strong magnetic field and are subjected to a radio-frequency field. Only those nuclei which have a non-zero magnetic moment (μ) and spin angular momentum (I) undergo resonance absorption. Over a hundred nuclei satisfy this condition, but there are many important isotopes which have zero spin angular momentum and zero magnetic moment. Thus, while n.m.r. does occur with nuclei such as ^{1}H, ^{19}F and ^{31}P, it does not occur with ^{12}C, ^{16}O and ^{32}S and nuclear resonance absorption cannot be observed with the latter nuclei. The relative signal strengths obtained with different nuclei also vary. Strongest signals are obtained with hydrogen ^{1}H and fluorine ^{19}F, whilst phosphorus ^{31}P is considerably weaker in intensity. The nitrogen ^{14}N nucleus has a spin $I = 1$ but its signals are weak in intensity.

As we can see from equation (1), there is a linear relationship between the resonance frequency ν and the magnetic field H_0. Spectra can, therefore, be expressed either as intensity of absorption plotted against frequency at constant field strength, or against magnetic field at fixed frequency. Because of the ease of obtaining good monochromatic sources of electro-magnetic radiation, it is usually the frequency which is fixed and the magnetic field which is varied. In Table 1 are shown the operating frequencies for a number of nuclei at a fixed magnetic field of 14,100 G. With an isolated nucleus the nuclear resonance absorption spectrum would consist of a single very sharp line corresponding to absorption of electro-magnetic radiation at the magnetic field H_0. In a solid, interactions from other nuclei modify this so that the magnetic field at any nucleus is the sum of the applied magnetic field plus the field due to neighbouring nuclei. In this case a particular nucleus can, therefore, be

in a total magnetic field significantly lower or higher than the applied field. Thus the absorption spectrum of a solid is usually broad and of the order of several gauss wide. In a liquid, on the other hand, the molecules are in a state of violent thermal agitation and the fields contributed by the different nuclei are averaged out. The absorption lines from liquids are usually narrow and the line width is determined mainly by the inhomogeneity of the applied magnetic field.

In this book we are concerned entirely with molecules present in the liquid or solution condition. The n.m.r. spectrum of molecules in these states are determined by three main effects, (*a*) the chemical shift), (*b*) the

TABLE 1. Physical Constants of Some Common Nuclei

Nucleus	Natural abundance, %	Spin I	N.M.R. frequency (in Mc/s) in 14,100 G field
^{1}H	99·98	$\frac{1}{2}$	60·00
^{2}H	0·015	1	9·21
^{10}B	19	3	6·45
^{11}B	81	$\frac{3}{2}$	19·27
^{12}C	98·9	0	—
^{13}C	1·1	$\frac{1}{2}$	15·10
^{14}N	99·6	1	4·34
^{16}O	99·8	0	—
^{19}F	100	$\frac{1}{2}$	56·5
^{31}P	100	$\frac{1}{2}$	24·3

spin coupling interaction, (*c*) exchange effects. Relaxation effects are also important. We shall now describe and discuss, in this order, each of these effects.

Chemical Shift

The field at a nucleus due to the field of the magnet is modified by the induced diamagnetic electronic currents. These set up a secondary magnetic field so that if H_0 is the field in the bulk of the specimen the field actually experienced by the nuclei is

$$H = H_0(1-\sigma') \tag{2}$$

where σ', the screening constant, is characteristic of the electronic environment of the nuclei. With nuclei in different chemical positions, the value of σ varies. The displacement of resonance produced by the additional field at the nucleus is proportional to the strength of the applied field and is called the chemical shift. The chemical shift δ is a measure of the difference between values of σ' for different chemical positions.

The screening constants are small in value, and are smaller for protons than for most other nuclei. The latter is due to the fact that the total number of electrons in the immediate vicinity of a proton is so much smaller than for any other nucleus. It is customary to use shielding constants such that

$$\sigma = \sigma' \times 10^6 = \frac{H - H_{\text{ref}}}{H_{\text{ref}}} \times 10^6 \tag{3}$$

where H is the field at which resonance occurs and H_{ref} the field at which the nucleus in the reference surroundings gives resonance at the same frequency.

Chemical shifts δ are then given as

$$\delta = \sigma_1 - \sigma_{\text{ref}} = \frac{H - H_{\text{ref}}}{H_{\text{ref}}} \times 10^6 \tag{4}$$

With protons a very convenient reference compound is tetramethylsilane and the quantity $\tau = 10 - \delta$ has been introduced so that

$$\tau \text{ (p.p.m.)} = 10 - \frac{\Delta(\text{Me}_4\text{Si}) \times 10^6}{\text{oscillator frequency (c/s)}} \tag{5}$$

Δ is the displacement in frequency between the sample resonance and the Me_4Si resonance. On this scale τ is positive for all but very acidic

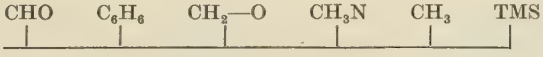


FIG. 2. Typical chemical shift positions for protons in various environments.

protons. This is the scale now widely used for work with protons and will be used in all our subsequent discussions. Most commercial instruments now have precalibrated charts which enable chemical shift values to be read directly. Some typical chemical shift positions for protons in various environments are shown in Fig. 2.

PROTON CHEMICAL SHIFTS

Although it might be expected that the screening of the proton might be proportional to the local electron density, this is not the case. The screening depends more on electronic currents induced in other parts of the molecule. The diamagnetic currents in the molecule can be divided into two contributions, intra- and inter-atomic. The intramolecular currents are localized circulations in individual atoms and lead to approximately additive contributions. The inter-atomic currents can play an important role in the magnetic properties of molecules with a

cyclic structure, particularly aromatic molecules in which mobile electrons are partly free to move around closed conjugated paths.

Protons in simple paraffins are the least deshielded and the protons of

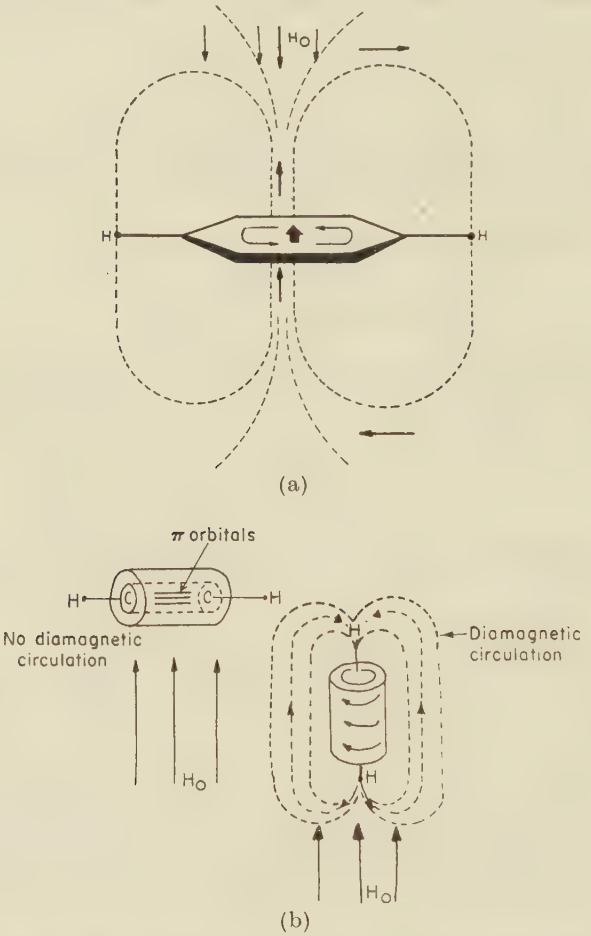


FIG. 3. (a). The ring current induced in benzene by a magnetic field. This gives rise to a diamagnetic moment perpendicular to the plane of the ring and opposite in direction to the component of the external field.

(b) The shielding of acetylenic protons due to diamagnetic anisotropy.

methyl groups are about 0·3 p.p.m. more screened than those in CH_2 groups. Protons attached to carbon–carbon double bonds appear considerably further to low field. The smaller screening of these protons is consistent with the reduction of charge on the hydrogen atom which is thought to occur following the change from sp^3 to sp^2 hybridization.

Because of the presence of ring currents that flow through the π molecular orbital system in aromatic hydrocarbons, the chemical shift of these protons occurs at low applied fields. This is because the secondary magnetic field due to the ring current reinforces the primary field at the position of the protons, so that a lower applied field is required to induce resonance. The ring current acts in an anti-screening manner. This is illustrated in Fig. 3a. The position of acetylenic protons is somewhat anomalous and its chemical shift is found to occur between those found for sp^3 and sp^2 hybridization situations. This is because diamagnetic circulation of electrons in the C≡C bond can occur more easily if the magnetic field is along the axis of the molecule. This is illustrated in Fig. 3b. Aldehydic protons also have an anomalous low field position. This can also be explained in terms of diamagnetic anisotropy.

Additivity rules. Because proton chemical shifts can be determined by the magnetic anisotropy of neighbouring groups it is possible to give a list of shielding constants which can be used to predict the chemical shift of protons adjacent to two or three anisotropic groups. Some of these shielding constants are shown in Table 6. Because the magnetic field of a neighbouring anisotropic group depends on direction as well as distance, sometimes the predicted values using these shielding constants are not too good, and deviations occur, especially in cyclic compounds. Some examples of the use of the shielding constants are given below.

Examples:

(i) $C\underline{H}_2Cl_2$	(ii) $CH_2{=}CMe.C\underline{H}_2.CMe_3$	(iii) $(C_6H_5.C\underline{H}_2)_2O$
Methylene chloride 4·67 (calc. 4·78) τ	2,4,4-Trimethylpent-1-ene 8·09 (calc. 8·05) τ	Dibenzyl ether 5·51 (calc. 5·65) τ

See in Correlation tables, Shoolery's Rules, Table 6.

Spin–Spin Coupling and Classification of Nuclear Groups

The second important effect is the one due to the effect of spin–spin coupling between nuclei. This arises as a result of the interaction of one nuclei with another probably via electron structure of the intervening bonds.

The common example to illustrate this effect is shown in the n.m.r. spectrum of ethyl alcohol (Fig. 4). Under lowish resolution, determined by the magnetic field homogeneity, three lines are observed corresponding to the chemical shift values of the protons in the different chemical groups in the molecule, OH, CH_2 and CH_3, with line intensities in the ratio 1:2:3 respectively corresponding to the number of protons within each group. With greater resolution, however, considerable multiplicity is observed and four lines are observed corresponding to the CH_2 group

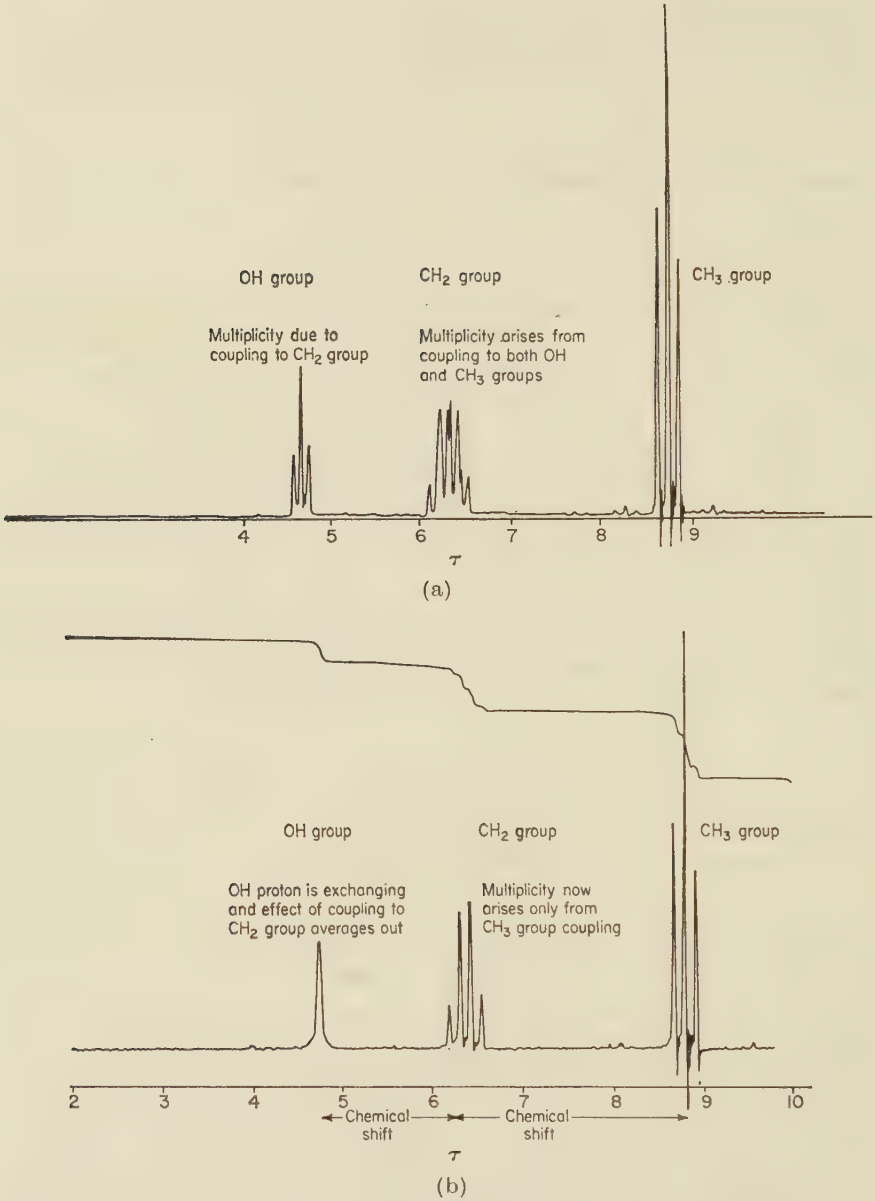


FIG. 4. (a) The high resolution n.m.r. spectrum of ethyl alcohol showing the chemical shifts of the different types of proton and the fine structure due to spin–spin coupling.

(b) In the presence of alkali the OH proton exchanges so coupling to CH_2 group is averaged. (The integral trace is shown.)

absorption, and three lines corresponding to the CH_3 group absorption. (With greater resolution further lines are observed as a result of second-order spin–spin couplings.) Unless the ethyl alcohol is carefully dried the signal from the OH group remains single. This additional fine structure is not a chemical shift phenomenon, since, on observing the spectrum at different values of the magnetic field, the spacings within the three-line and four-line multiplets remain unaltered, whilst the spacing of the principal lines of the methylene, methyl and hydroxyl groups can be made greater or smaller, dependent upon the value of the magnetic field. The spacings within the CH_2 multiplet and CH_3 multiplet are the same and are indicated by J, the spin–spin coupling constant and are measured in units of cycles per second.

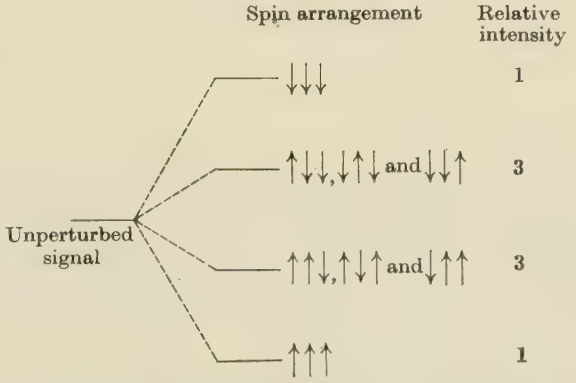


FIG. 5. The splitting of the methylene group proton signal by spin–spin interaction with methyl group protons showing the spin arrangements.

We can see how the multiplicity arises for an ethyl group by means of the following simple considerations. The two methylene protons can have any one of four possible combinations of their magnetic quantum numbers, one way to give $+1$, two ways to give zero and one to give -1. Thus the methyl protons will "feel" one of three effective fields, depending upon the instantaneous spin arrangement of the methylene group. Hence the methyl resonance will be split into a triplet of intensity 1:2:1. Similarly the methylene protons will "feel" the effective fields of the four possible instantaneous spin arrangements of the methyl group and its signal will consist of four lines of intensity 1:3:3:1. This is illustrated in Fig. 5. The lack of multiplicity of the hydroxyl proton signal and any further splitting of the methylene group signal in the spectrum of ethyl alcohol is due to rapid exchange of the hydroxylic protons. The hydroxylic proton will, in a given interval of time, be attached to a number of

different ethanol molecules and will, therefore, experience all possible spin arrangements of the methylene group. If the chemical exchange occurs with a frequency greater than the frequency separation of the components of the multiplet from the hydroxylic proton, the magnetic effects are averaged and a single sharp absorption line is observed.

We can see that this multiplicity in ethyl alcohol is an example of a more general situation. Thus if we consider the more general case of a proton, or other magnetic nucleus of spin $\frac{1}{2}$ with n equivalent neighbours, then its resonance will be split into $(n+1)$ fine structure lines with relative intensities given by the coefficients of the various terms of a binomial expansion of the type $(x+y)^n$, e.g.

$$\begin{array}{ll} n = 1 & 1:1 \\ n = 2 & 1:2:1 \\ n = 3 & 1:3:3:1 \\ n = 4 & 1:4:6:4:1 \end{array} \qquad (6)$$

In general, the effect of one proton on the resonance of another proton, or group of equivalent protons, depends upon the number and kind of intervening chemical bonds and upon the stereo-chemical relations of the interacting groups. The splitting for non-equivalent protons in saturated systems is about 15 c/s when on the same carbon, about 5 to 8 c/s when on contiguous carbon atoms, and zero when separated by more than two carbons. The splitting of phosphorus can extend over as much as two bonds. Chemically equivalent hydrogen nuclei do not cause mutual multiplicity. The effect of restricted rotation can cause apparently equivalent protons to become, in fact, non-equivalent. Values of spin coupling constants for different situations are shown in Part II, Table 34.

This simple multiplicity relationship only occurs when the spin coupling constant is small compared to the chemical shift difference (as in AX cases) between the two resonance signals. If these two are comparable, complex patterns are obtained which have to be analysed by appropriate quantum mechanical calculations of the energy levels and spectroscopic transitions.

Fortunately many of these complex patterns have been calculated by solution of the Schrödinger wave equation for a range of parameters.[1]

Thus if J and σ are known, spectra containing many lines can readily be calculated. If these parameters are not known, spectra can be calculated until a satisfactory fit to the experimental spectrum is obtained.[11]

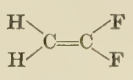
The basis of the calculations lies in the solution of the Schrödinger wave equation

$$\mathscr{H}\psi = E\psi \qquad (7)$$

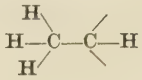
where ψ is the wave function which describes the condition of the nuclear spins and $\mathscr{H}$ is the Hamiltonian which operates on ψ in order to quantize the energy function.

The Hamiltonian includes a term for the interaction of the nuclear magnet with the external field and for the electron coupled spin–spin interaction.

A nuclear resonance notation has been introduced for typical groups of nuclei which occur in molecules. Thus symbols A, B ... are used for non-equivalent nuclei of the same species whose relative chemical shifts are of the same order of magnitude as the spin coupling between them. Equivalent nuclei are described by the same symbol, e.g. A_2, B_4, etc. The symbols X, Y are used for another set whose signals are widely separated from those of the set A, B ... and the nuclei may or may not be of the same species. Examples of the nomenclature are:



A_2X_2



AB_3

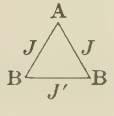
The AB system. This is the simplest system of two non-equivalent nuclei in which the effects of chemical shift and spin coupling intermingle. At one extreme we have the AX system which gives rise to a pair of doublets of equal intensity, whilst at the other extreme we have the A_2 system giving rise to a single line. The intermediate situation, in which the chemical shift δ_{AB} between the nuclei is similar to the spin coupling constant J_{AB}, also consists of a pair of doublets but the intensities of the four lines are no longer equal. This system requires theoretical analysis.

The general appearance of the spectrum depends only upon the ratio J/δ_{AB} and is independent of the signs of J and $\sigma_B - \sigma_A$. The spectrum for some values of this ratio are shown in Fig. 6. With the lines labelled as shown, the following relations hold

$$(3-4) = (1-2) = J_{AB} \text{ in cycles}$$
$$(1-3) = (2-4) = \sqrt{\{(\delta_B - \delta_A)^2 + J_{AB}^2\}} \qquad (8)$$

From these $\delta_B - \delta_A$ can be determined and hence δ_A and δ_B. See example 3, p. 57.

AB_2 systems. The energy level system for AB_2 has been calculated by a number of workers. There are two different spin-coupling constants J and J'



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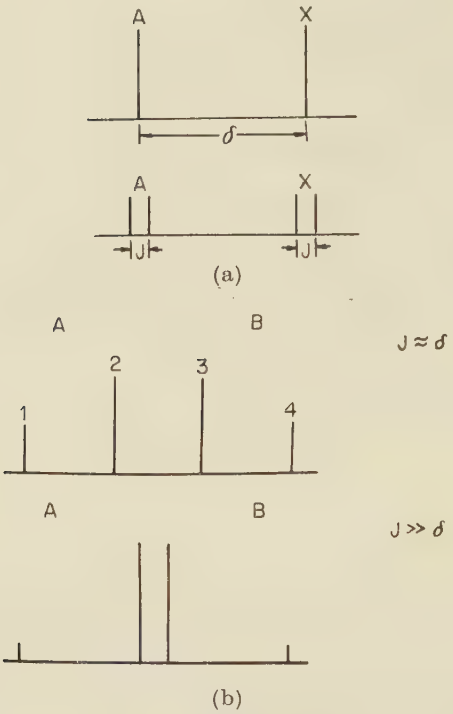


FIG. 6. (a) Typical spectra for two nuclei AX uncoupled and coupled (lower). (b) Typical spectra for two nuclei AB for differing values of R ($=J/\delta$).

There are eight energy levels and nine allowed transitions. The appearance of the spectrum depends only on the ratio of J_{AB}/δ_{AB} and is independent of J'_{BB} (see Fig. 7). At large chemical shift differences the spectrum is of an AX_2 type. Here the A lines 2 and 3 coalesce and the A resonance becomes a symmetrical triplet of relative intensities 1:2:1

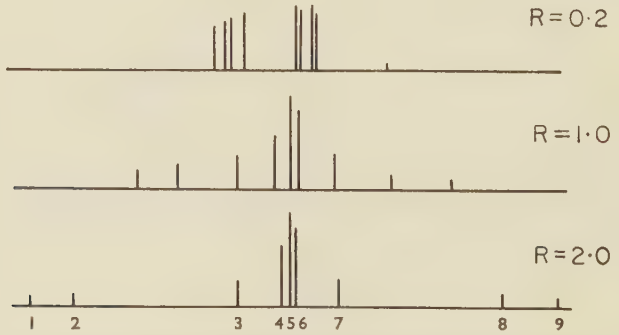


FIG. 7. Typical spectra for three nuclei AB_2 at different values of R ($=J/\delta$).

and spacing J_{AB}. The B lines 5, 6, 7 and 8 also coalesce to a doublet of spacing J_{AB}.

When J/δ_{AB} is of the order of 1, no pair of lines is separated simply by J_{AB} or by δ, and for the qualitative identification of the nine AB_2 lines in a spectrum one can use the following rules derived from the calculated transition energies:

(*a*) The chemical shift position of proton A can be derived directly from the position of line 3.

(*b*) The chemical shift position of protons B is given by the arithmetic mean of lines 5 and 7 which is identical with the arithmetic mean of lines 2 and 9.

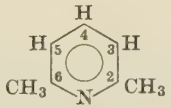
(*c*) J_{AB} can be obtained from the relationship (when $J_{AB} \geqslant 0$)

$$J_{AB} = \tfrac{1}{3}[\nu_4+\nu_8-\nu_1-\nu_6] \tag{9}$$

(*d*) Other relationships have been found to occur (when $J_{AB} \geqslant 0$)

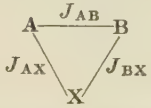
$$\begin{aligned} \nu_1-\nu_4 &= \nu_5+\nu_6-\nu_7-\nu_8 \\ \nu_1-\nu_2 &= \nu_3-\nu_4 = \nu_6-\nu_7 \\ \nu_2-\nu_5 &= \nu_4-\nu_8 = \nu_7-\nu_9 \end{aligned} \tag{10}$$

The protons in the molecule 2,6-lutidine are an example of an AB_2 system ($H_4.[H_5H_3]$)



In practice the spectrum is calculated for selected values of the ratio J/δ_{AB} until the best over-all fit is obtained.

ABX systems. The spectrum of a simple AB system is modified if one or both nuclei are coupled to a third nucleus X. The system ABX, in fact, gives rise to fourteen lines, of which four can be considered A transitions, four B transitions, four X transitions, and two weak combination lines. There are three coupling constants as shown



Spectra of this type are readily interpreted if we consider J_{AX} and J_{BX} as perturbations of the AB and X resonances. We see then that the four lines present in the AB spectrum which we have just discussed are each split into a doublet. This gives a spectrum of the type shown in Fig. 8a.

The coupling constant J_{AB} is equal to the separation between lines 1 and 3 and 5 and 7. The two A lines are separated by

$$\nu_8-\nu_7 = \nu_6-\nu_5 = \tfrac{1}{2}(J_{AX}+J_{BX})+C_{ABX} \tag{11}$$

and the two B lines are both split by

$$\nu_2-\nu_1 = \nu_4-\nu_3 = \tfrac{1}{2}(J_{AX}+J_{BX})+C_{ABX} \tag{12}$$

where C_{ABX} is a quadratic function of $\delta_{(AB)}$, J_{AB}, J_{AX} and J_{BX}. When $J_{AX}=J_{BX}$ it has the value zero.

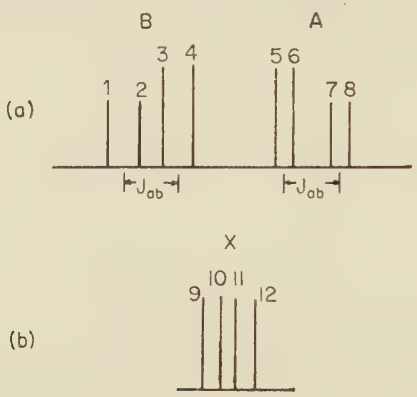
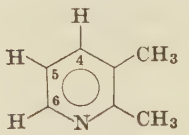


FIG. 8. The ABX spectrum: (a) the A and B lines, (b) the X lines.

The X spectrum (Fig. 8b) is a symmetrical quadruplet with splittings equal to those given for the AB resonance. This is shown in the following relationships.

$$\begin{aligned}\nu_6-\nu_5 &= \nu_8-\nu_7 = \nu_{10}-\nu_9 = \nu_{12}-\nu_{11}\\ \nu_2-\nu_1 &= \nu_4-\nu_3 = \nu_{11}-\nu_9 = \nu_{12}-\nu_{10}\end{aligned} \tag{13}$$

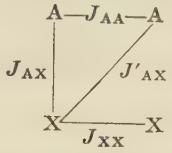
The ring protons of 2,3-lutidine are an example of an ABX system



The signals from the H_6 protons are well separated from those of H_4 and H_5.

A_2X_2 and A_2B_2 system. The spectra of the A_2X_2 and A_2B_2 systems consist of two bands each containing a maximum of ten and twelve lines respectively. The spectra of both systems are symmetrical so that in the A_2B_2 systems the set of twelve A lines is always the mirror image of the

twelve B lines. In the A_2X_2 case the A and X bands are themselves symmetrical. There are four coupling constants as shown



It can be seen that couplings between structurally equivalent protons J_{AA} and J_{XX} are important in determining the spectrum. The simplest spectrum occurs when the AB coupling constants are equal ($J_{AB}=J'_{AB}$).

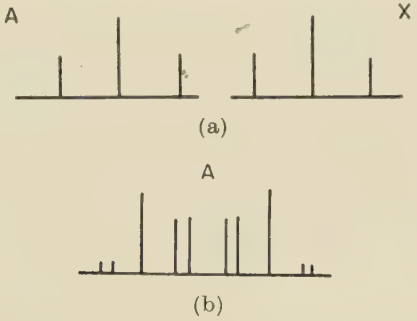


FIG. 9. The A_2X_2 spectrum: (a) where $J_{AB}=J'_{AB}$. (b) the A part of the spectrum when $J_{AB}\neq J'_{AB}$ and $J_{AA}>J_{BB}>0$.

If, also, the chemical shift is large as occurs in an A_2X_2, some transitions are forbidden and many of those remaining are degenerate, so the spectrum consists of two 1 : 2 : 1 triplets. This is shown in Fig. 9a. The spectrum is independent of $J_{AA'}$ and $J_{BB'}$ and the separation between the components of each of these triplets is equal to J_{AB}.

The A-half of the A_2X_2 spectrum gives rise to ten lines in a symmetrical pattern when $J_{AB}\neq J'_{AB}$ and $J_{AA}>J_{BB}>0$. This is shown in Fig. 9b. The X-half is identical with the A-half. Under the same conditions the A_2B_2 spectrum contains twenty-four lines. The common feature of A_2X_2 spectra is the symmetrical nature of the bands.

The A_2B_2 systems are more complicated than the A_2X_2 systems and vary widely with different sets of coupling constants. The patterns of the

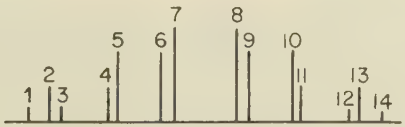


FIG. 10. A typical A_2B_2 spectrum when $J_{AB}=J'_{AB}$.

bands now depend upon σ_{AB} as well as the four coupling constants. When $J_{AB}=J'_{AB}$ a simplification occurs and seven lines are observed within each band, see Fig. 10. The chemical shift resonant positions of the two nuclei are given directly from lines 5 and 10.

Some examples of A_2B_2 spectra have been observed with 1,2-dichlorobenzene and naphthalene.

AB_3 systems. The AB_3 grouping often occurs in the form of the grouping

$$CH_3—CH$$

and we will consider it briefly. The methyl group is usually rotating rapidly about its three-fold axis of symmetry and the three AB coupling constants have the same average value. Such a system has sixteen allowed transitions of the B nucleus. When the coupling value is small (5–7 c/s) only a broad envelope is observed and the individual lines are not resolved. At large chemical shift in an AX_3 system the X_3 band consists of a doublet of equal intensity. At low values of J_{AB}/δ_{AB} the low frequency line increases in relative intensity compared with the other component. At high values the high frequency line only appears as an inflexion on the side of this component. The A lines and B lines also overlap at this stage.

A useful book for comparison of theoretical and experimental spectra is available.[11]

COUPLING CONSTANTS AND STRUCTURE

Spin–spin coupling constants vary in characteristic ways dependent upon the structure. Theoretical explanations for some of these effects are still not completely understood but the values can be used in an empirical way to provide information about the structure of unknown molecules.

We can make the following comments about these relations:

(*a*) There is usually a rapid decrease in coupling constant with an increase in the number of chemical bonds separating the protons. Thus the coupling between protons separated by more than two other saturated atoms is usually very small (< 1 c/s). The coupling of *ortho* protons is usually greater than *meta* which in turn are greater than *para* protons.

(*b*) In double-bonded systems the coupling constants are usually in the order $J_{trans} > J_{cis} > J_{gem}$.

(*c*) Theoretical calculations (Fig. 11a) predict that the coupling constant J between protons within a methylene group is a sensitive function of H—C—H angle. J decreases from 20 c/s at a bond angle of 105° to zero when the bond angle is 125°. Experimental values are in fairly good agreement with the calculated curve.

(*d*) Theoretical calculations of vicinal protons as in ethane predict that $J_{HH'}$ will depend upon the angle ϕ between the HC—C′ and C—C′—H′ planes, so that the coupling is a maximum at dihedral angles

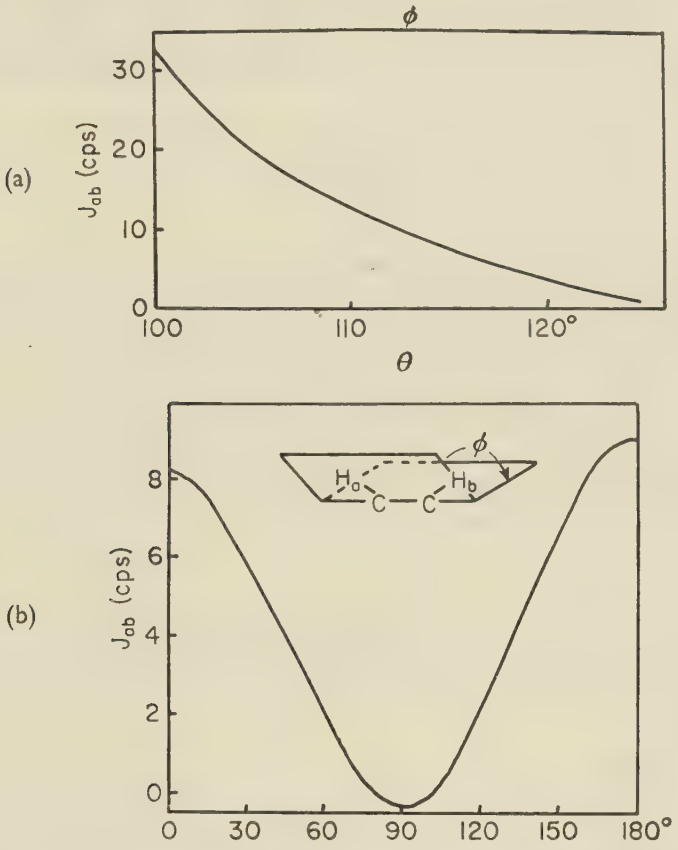


FIG. 11. Calculated values of J_{AB} in the structures (a) $C\begin{matrix}H_a\\H_b\end{matrix}$ and (b) as a function of the dihedral angle ϕ in $CH_a—CH_b$

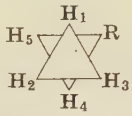
of 0 and 180°, and a minimum at a dihedral angle of about 90°. This is illustrated in Fig. 11b.

(*e*) In substituted cyclohexanes the axial–axial coupling is larger than axial–equatorial or equatorial–equatorial.

Some useful values of proton–proton and proton–fluorine spin coupling constants are given in Tables 34 and 35 (Part II).

Internal Rotation

In ethyl alcohol the methyl group can freely rotate about the C—C bond and the protons within the group are equivalent. We can see that this is so by considering the molecule CH_3CH_2R. The molecule has three rotational isomers of equal energy and population. The staggered configurations are assumed to be more stable than the eclipsed form. One of the *trans* forms is:



At slow rotation of the methyl group the spectrum is typical of one structure. Proton H_2 will have a different screening constant than H_1 and H_3. Protons H_4 and H_5 will have the same screening constant. If the chemical shifts are large enough the spectrum would show three types of protons and be of the type AB_2X_2. At rapid rotation the screening constants become equal and the spin coupling constants between any hydrogen on the CH_3 group and the protons of the CH_2 group become equivalent. Thus for rapid rotation the spectrum becomes of the type A_2B_3 with all AB coupling constants equal.

Information about the rate of rotation can be provided from the spectra.

The possibility of internal rotation occurring, and also the hindering of rotation, must always be considered in the interpretation of the spectra. The non-equivalence of what superficially may be equivalent nuclei must always be considered.

Exchange Effects

In many organic molecules the protons are not firmly attached and rapid exchange of the proton from one group to another group within the molecule, or from the molecule to a solvent, can occur. An example of exchange effects is observed in the spectrum of ethyl alcohol when a trace of alkali is added, see page 10. This exchange behaviour also occurs with mixtures of alcohols and water.

If protons are moving between two environments A and B they have an average residence time τ_A and τ_B at each site. These are given by

$$\tau_A = 1/K_A \quad \text{and} \quad \tau_B = 1/K_B \tag{14}$$

where K_A and K_B are the first-order rate constants for exchange. Even when a chemical shift difference occurs between the two protons, if the residence times are short, only a single absorption line is observed

corresponding to a weighted average of the resonant frequencies (corresponding to the "resident" proton chemical shift).

When the values $\tau_A = \tau_B = \tau$, the populations at both sites are equal. With larger chemical shift or longer residence times, separate resonance lines will be observed where δ_e, the observed chemical shift, is given by

$$\delta_e = \delta_\nu[1 - 2\int(\tau\delta_\nu)^2]^{1/2} \qquad (15)$$

where δ_ν is the chemical shift between the protons in the two environments. The activation energy for the process can be determined by measuring δ_e, and therefore τ as a function of temperature.

Relaxation Effects

When the nuclei have absorbed radiation and have been excited to the upper energy level there are a number of ways in which the nuclei can return to the lower state. Thus radiationless transitions can occur in which nuclei can exchange energy with their environment. The various ways in which this can occur are called relaxation processes. These processes are of great importance for nuclear resonance absorption. They are responsible for the maintenance of the absorption condition and also control the lifetime expectancy of a given state. From the uncertainty principle $\left(\Delta H . \Delta t = \frac{h}{2\pi}\right)$ the "natural" width of a spectral line is proportional to the reciprocal of the average time the system spends in the excited state. Without interaction between the system of nuclear spins and the surroundings or lattice, the resonance absorption would continue only until the populations were equal. The "cooling" of the nuclear spins is called spin–lattice relaxation.

Relaxation processes are of two types, spin–lattice relaxation and spin–spin relaxation. The term lattice is used to describe the entire molecular system irrespective of the physical state of the material. In spin–spin relaxation a nucleus transfers its energy to a neighbouring nucleus of the same isotope by a mutual exchange of spin. In spin–lattice relaxation the energy of the nuclear spin system is converted into thermal energy of the molecular system.

The efficiencies of these processes are expressed as relaxation times. Thus the spin–lattice relaxation time T_1 is the half-life required for a perturbed system of nuclei to reach an equilibrium condition. A large value of T_1 indicates an inefficient relaxation process. Most purified solids have very long values of T_1 often of the order of some hours at low temperatures. For organic liquids T_1 is of the order of one second. The spin–spin relaxation time T_2 is the time constant measuring the rate at

which the precessing nuclei get out of phase with one another and is determined by the magnetic spread within the sample. The value of T_2 can be determined from the line width.

In the spectra of organic molecules each peak in the spectra will usually have a different relaxation time. The relaxation of a given proton is affected by the molecular motion of neighbouring protons. The contribution to the relaxation rate is proportional to the inverse sixth power of the distance $\left(\frac{1}{T_1} \propto \frac{1}{r_0^6}\right)$.

The spin–lattice relaxation times are affected by the presence of paramagnetic molecules or ions in the sample. The n.m.r. lines of paramagnetic substances are, therefore, very broad.

Those nuclei with a spin quantum number $I > \frac{1}{2}$ mostly possess an electric quadrupole moment. Such nuclei frequently exhibit very short spin–lattice relaxation times and the absorption lines associated with these nuclei are broad in appearance.

3. Uses of Nuclear Magnetic Resonance Spectroscopy

The applications of high resolution n.m.r. spectroscopy are, of course, being continuously enlarged. However, the major use of the technique for the organic chemist is to confirm the structure of some compound which he may have prepared, or to provide information about the structure of unknown materials. He may also be concerned with rate processes. The biochemist may also be interested in the interaction of one molecule with another and the n.m.r. technique can also be useful for this purpose.

Identification of a Substance

The n.m.r. spectrum of a compound is characteristic of the compound and can be used for identification just as the melting point, boiling point, infra-red spectrum, X-ray powder photograph and other physical constants are used. The n.m.r. spectrum is often useful alone but is more useful when used with data obtained by other techniques, including infra-red and ultra-violet spectroscopy and mass spectroscopy. The particular feature of a high resolution n.m.r. spectrum arises from the transparency of many nuclei, so that if we are looking at the proton resonance spectrum, only the protons in the molecule give rise to the resultant spectrum. These signals may of course be modified by the presence of other magnetic nuclei. We can then look separately at the fluorine or phosphorus resonance spectrum. The n.m.r. spectrum is, therefore, not as unique as an infra-red spectrum where the absorption facts are determined by vibration of the whole molecule. On the other hand, it is quite usual to be able to identify and locate every grouping in an n.m.r. spectrum, whereas this is rarely the case with an infra-red spectrum.

Spectral studies are usually carried out with dilute solutions or with the material in a liquid condition. Studies of the liquid are limited by viscosity effects which affect the relaxation times and tend to cause broadening of the resultant lines. Signals can be obtained with gaseous samples but, because of the difficulty of obtaining adequate signal strength, this is less frequent. In general it is necessary to use as concentrated a solution as possible, remembering that the chemical shifts

of some lines can be a function of concentration. This effect is usually not large but in extreme cases can amount to several parts per million and can vary for different groups within the same molecule.

The use of n.m.r. spectroscopy for determining the types of functional groups which are present in a molecule is determined by the chemical shift values on some arbitrary scale. This is often done with proton resonance spectra using as a reference the material tetramethylsilane which is given the arbitrary value of 10. The connection between the chemical shift value and structure is largely empirical and so it is necessary to have correlation tables for the most effective use of this branch of spectroscopy. We have presented for this purpose a number of these correlation tables in the second part of the book. The signals can also be integrated so that the number of protons in the different functional groups can be measured. Here the n.m.r. technique has an advantage over other spectroscopic methods in that the intensities are proportional to the number of nuclei in a given environment so that there are no extinction coefficients to be determined. The additional fine structure which is observed in the n.m.r. spectrum which arises from spin coupling can be used to provide information about neighbouring groups within the molecule, so that an analysis of this fine structure can provide useful information about the position of particular functional groups with respect to each other in a molecule. The values of the spin coupling constants can also be useful.

Briefly then there are three main pieces of information which can be obtained from a typical high resolution n.m.r. spectrum.

(*a*) The line position, or the *chemical shift value* index, provides information about the molecular environment of the protons contributing to the peak. Protons in similar chemical environments in different molecules show similar chemical shift values. Using the correlations of chemical shift values for protons in different environments, particular functional groups present in the molecule can be deduced.

(*b*) The intensity of a peak within a spectrum is directly proportional to the number of protons contributing to the peak. Thus the relative numbers of protons in different chemical environments can be determined.

(*c*) The fine structure or splitting pattern associated with the absorption lines and arising from spin–spin coupling, provides information on the spatial relations and numbers of neighbouring nuclei.

Further information can be obtained by separately observing a spectrum of another magnetic species within the molecule. Complex spectra with overlapping lines can be simplified by spin decoupling techniques using double irradiation techniques (see page 42). Different

solvents and isotopic substitutions can also help to provide a better interpretation of the spectral data.

Reaction Kinetic Studies

Nuclear magnetic resonance spectroscopy is very useful for studying various rate processes which can occur with organic molecules. In a system where a hydrogen atom is not firmly attached, so that reversible proton exchange can occur, it is possible to determine the kinetics of the reaction. In other cases the molecule may be non-rigid and exist in a state of equilibrium between a number of possible conformations. The rate process of this type of reaction can also be obtained.

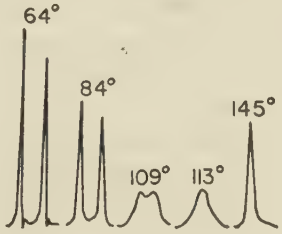


FIG. 12. The n.m.r. spectrum of the methyl groups of dimethylformamide at varying temperatures.

An example of hydrogen atoms exchanging is observed with acetic acid in water. Whilst we might expect to be able to observe signals from both the carboxyl protons and water protons using chemical shift data, in fact only one line appears. This line has a position intermediate between the carboxyl proton and water proton resonances. This means that the rate of protolysis is high and the single resonance line corresponds to the average environment of the proton. Molecules such as glycine have also been studied in aqueous solution and the exchange of protons investigated by means of the effect upon the n.m.r. spectrum of the methylene group. This has been carried out at various pH values.

Cyxlohexane and its derivatives are molecules which undergo rate processes involving the non-rigid molecules. Separate signals can be observed from equatorial and axial protons when interchange between the conformations is not possible. As the temperature changes the separate signals merge corresponding to the average environment of the protons in the cyclohexane ring. Rotation about CN bonds in amides has also been studied; thus dimethylformamide has two methyl groups

which are non-equivalent when there is no rotation about the CN bond. As the temperature increases so does the rate of internal rotation, and the two signals collapse at about 100°C to a single peak (Fig. 12). The rate of internal rotation can be calculated from the signal shape of the barrier surrounding internal rotation determined from the variation of rate with temperature.

Fundamental Studies

The number of fundamental studies using high resolution n.m.r. spectroscopy are rapidly increasing and we shall only instance a few examples here. Thus the technique has been used to provide information about the electronic structure of molecules. The calculation of fine structure in the spectra by quantum mechanics is itself a check on our understanding of the properties of the atoms or nuclei in molecules. The non-sphericity of the electric charge distribution within a nucleus or its electric quadrupole moment can be studied by its effect on nuclei attached to it. Relaxation measurements have been used to provide an indication of the orientation and behaviour of molecules in liquids or in solution, or to study the interactions of one molecule with another.[12]

By studying n.m.r. spectra in nematic liquid crystals, proton-proton distances have been determined and information about liquid crystals determined. The degree of delocalization of unpaired electrons in conjugated systems and their spin densities have been determined by studying transition metal complexes. The physical state of water around ions or in biological situations has also been studied.

4. Experimental Techniques

Instrument Design

The apparatus required for n.m.r. spectroscopy consists essentially of four parts: (*a*) a magnet for producing a strong homogeneous field to produce the non-degenerate energy levels for nuclear transitions; (*b*) a method for varying the magnetic field over a small range; (*c*) a radio-frequency oscillator to produce a source of monochromatic electro-magnetic radiation; and (*d*) a radio-frequency receiver used as a detector to indicate when electro-magnetic energy is absorbed by the sample.

Both electro-magnets and permanent magnets are used in n.m.r. spectroscopy. The essential requirement of the magnet for high resolution studies is that it should have a region in which the strength and direction of the magnetic field does not vary from point to point to an order of about 1 part in 10^8. Each type of magnet, electro-magnet or permanent magnet, has its own advantages and disadvantages. The advantage of an electro-magnet is that it can make it possible to examine more than one isotope, or determine the spectrum of the same isotope at different field strengths without altering the radio-frequency oscillator. A disadvantage of the electro-magnet is that it is difficult to obtain good stability in terms of resolution and field strength without elaborate and expensive equipment. The advantage of a permanent magnet is that, provided there is good thermostatting of the equipment, the homogeneous field is always present and the stability, in terms of field strength, is usually very good. No variation of field strength is, however, possible.

The radio-frequency oscillator is the source of electro-magnetic radiation used to stimulate the transitions and may be obtained from a highly stable crystal-controlled oscillator whose output can be multiplied to the desired frequency.

There are two methods of detection in use. In the first (single coil method) the measurement of the absorption or dispersion signal is carried out by the transmitter coil of the radio-frequency oscillator. A diagram of a spectrometer using the single coil system is shown in Fig. 13a. This use of a radio-frequency bridge works in a similar way to a Wheatstone bridge. The bridge network balances out the transmitter signal and allows the absorption or dispersion signal to appear as an out-of-balance e.m.f. across the bridge. Out-of-balance signals can be amplified, rectified and recorded. The absorption and dispersion signals differ in phase

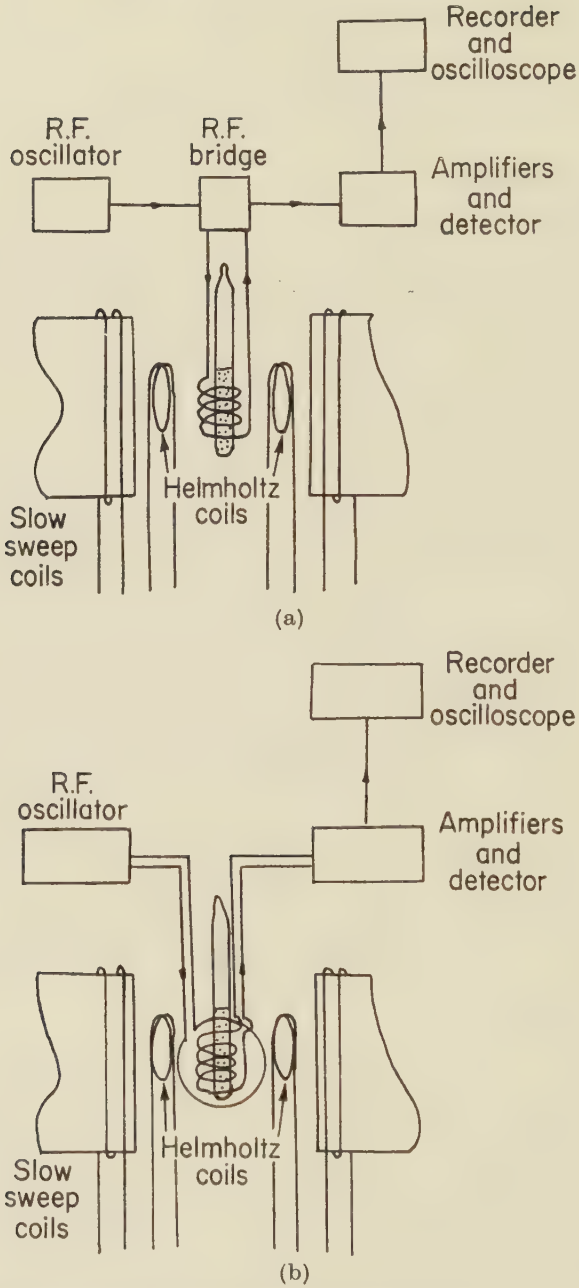


FIG. 13. Diagrammatic arrangement of n.m.r. spectrometer: (a) using the single coil system, (b) using the nuclear induction system.

by 90° and advantage is taken of this to suppress the dispersion signal. Thus, if the transmitter signal is not completely balanced out, and a certain amount of energy in phase with the absorption signal is passed by the bridge, the contribution of dispersion of the signal which is fed to the amplifier is negligible. The radio-frequency bridge is designed so that both phase and amplitude of the out-of-balance transmitter signal can be controlled. In this method only one coil is used to serve as both transmitter and receiver.

A second method of detection (double coil method) is sometimes called the nuclear induction method. A diagram of a spectrometer using the nuclear induction system is shown in Fig. 13b. In this case there are two coils with axes at right-angles to each other. In this way the transmitter signal is separated from the absorption and dispersion signals. Again some leakage of the transmitter signal, which is in phase with the absorption signal, can be effected so as to suppress the dispersion signal.

The rate at which the magnetic field is scanned can have a large effect on the shape of the absorption signals. Rapid sweeping can cause considerable distortion of the signal. The distortion is sometimes called "ringing" or "wiggles". This effect arises because of the finite relaxation time of the nuclei. The shorter the relaxation times, the less is the distortion due to ringing. The observation of ringing can be a good indication of a homogeneous field. The easiest way to remove unwanted ringing from recorded spectra is to use a slow sweep. On the other hand, saturation effects can limit the sweep rate.

The homogeneity of the fields between the pole faces of a magnet is greatest in the central region and falls off towards the edge. Thus, for the best resolution small samples are required. However, this has to be balanced against the strength of the absorption signal and the number of nuclei of a given type in the sample. A device which helps to reduce the effect of the large volume of the sample on the resolution is to spin the sample tube about the y-axis of the magnet system. For this to be effective, the spinning frequency has to be in excess of the required resolution when this is expressed in cycles/sec. If the spinning frequency is too low, averaging of the field is incomplete and the main absorption signal is accompanied by side bands. The spacing of the side bands are symmetric about the main band and equal the spinning frequency or some multiple of this. Very high spinning frequencies can also cause turbulence within the sample which can also affect the resolution.

Instruments Available

We list the instruments available in Table 2 and describe an example of each of the two main types of instrument. A cross-coil type of high

TABLE 2.

Model	Manufacturer	Nuclei available for examination	Resolution for protons	Typical sample vol.
A-60 A 56-60A	Varian Associates	Protons only ^{1}H and ^{19}F	0·4 c/s	0·2–0·4 cm^3
HA-100 HR-100	Varian Associates	^{1}H, ^{19}F, ^{31}P, ^{11}B, ^{13}C, ^{17}O	1 part in 2×10^8 corresponding to 0·5 c/s	0·4
HA-60/DA-60	Varian Associates	^{1}H, ^{19}F, ^{31}P, ^{11}B, ^{13}C, ^{17}O	1 part on 2×10^8 corresponding to 0·3 c/s	0·4
R.10	Perkin-Elmer	^{1}H, ^{19}F, ^{31}P, ^{11}B	Better than 1 in 10^8	0·45
RS.2	A.E.I.	^{1}H, ^{19}F, ^{31}P	Better than 1 in 10^8 for ^{1}H at 60 Mc/s	0·45
JNM-3H-60 JNM-3H-100	Japan Electron Optics Laboratory Co. Ltd.	^{1}H and ^{19}F without attachments ^{14}N and ^{11}B with attachments	5×10^{-9} (0·3 c/s)	0·4

resolution n.m.r. spectrometer is available from Varian Associates, Palo Alto, California, and uses electro-magnets with stabilized power supplies. The A-60 instrument is a specially designed analytical instrument which operates at a magnetic field strength of 14,092 G and at 60 Mc/s operating frequency. The resolution is 1 in 10^8. It features a control system which "locks" the magnetic field strength and the effective transmitter frequency. This enables the system to be very stable. It is locked in this way by means of a nuclear side-band oscillator which applies a modulation frequency of approximately 5 kc to the modulating coils in the sample probe. This produces two side-bands at 60 Mc/s $\pm$ 5 kc. At the control receiver the 60 Mc carrier is demodulated and 5 kc side-band signals remain. The upper side-band signal is applied to the input of the field modulator. This amplifies the audio voltage, and again applies it to the modulating coils, thus completing the loop. The circuit therefore attempts to remain in oscillation and shifts the side-band frequency to maintain just the right combination of field strength and

Instruments Available

Magnetic field	Stability	R.F. field at sample	Integral reproducibility	Operating frequency
14,092 G	Maximum rate of change of field homogeneity 1 c/h (Field frequency lock)	^{1}H–0·02–2·0 mG	2% when integrating spectra, 1% when integrating an external input	60 Mc/s
23,490 G	Ratio of field to frequency is maintained within 5 parts in 10^9 over a 1-h period with less than 1°C room temp. change from mean value, and less than ±10% line voltage fluctuation from normal	1 mG max. in proton stabilization mode. 0·5 mG to 5·0 mG variable in 1-dB increments without proton stabilization	2% when integrating spectra, 1% when integrating an external input	100 Mc/s
14,092	Ratio of field frequency is maintained within 5 parts in 10^9 over a 10-min period	5·0 mG to 50 mG, variable in 1-dB, increments in proton stabilization of conventional mode	2% when integrating spectra, 1% when integrating an external input	60 Mc/s
14,092 G	Drift less than 4 c/s/h	$3{\cdot}5\times10^{-2}$ mG to 2·8 mG	Within 2%	60 Mc/s
1000–17,500 G	Does not normally degrade more than a factor of 2 over a 12-h period		Within 2%	60 Mc/s
14,092 G 23,490 G	Field frequency stabilizer system			60 Mc and 50 Mc/s 100 Mc/s

effective transmitter frequency. This system enables preprinted charts to be used and spectra can be obtained on a routine basis. An integrator is attached and the integral can be recorded on the spectrum for direct correspondence. This instrument is only suitable for protons. Temperature studies can be readily made with this instrument.

A single-coil type spectrometer is the Perkin-Elmer R10 instrument. This is a permanent-magnet type instrument having a field strength of about 14,092 G corresponding to 60 Mc/s for protons of 1 in 10^8 with a field drift of less than 4 c/s. The spectrum is recorded on preprinted charts calibrated in c/s. Using an internal standard tetramethyl silane, chemical shift values can be determined directly to 0·1 c/s. Interchangeable frequency sources for hydrogen, fluorine, phosphorus, boron and nitrogen can be obtained. Maximum resolving power is assisted by means of Golay coils fitted at the pole faces. Both of these instruments operate at 60 Mc/s.

Recently a new instrument, the HR 100, has been introduced by

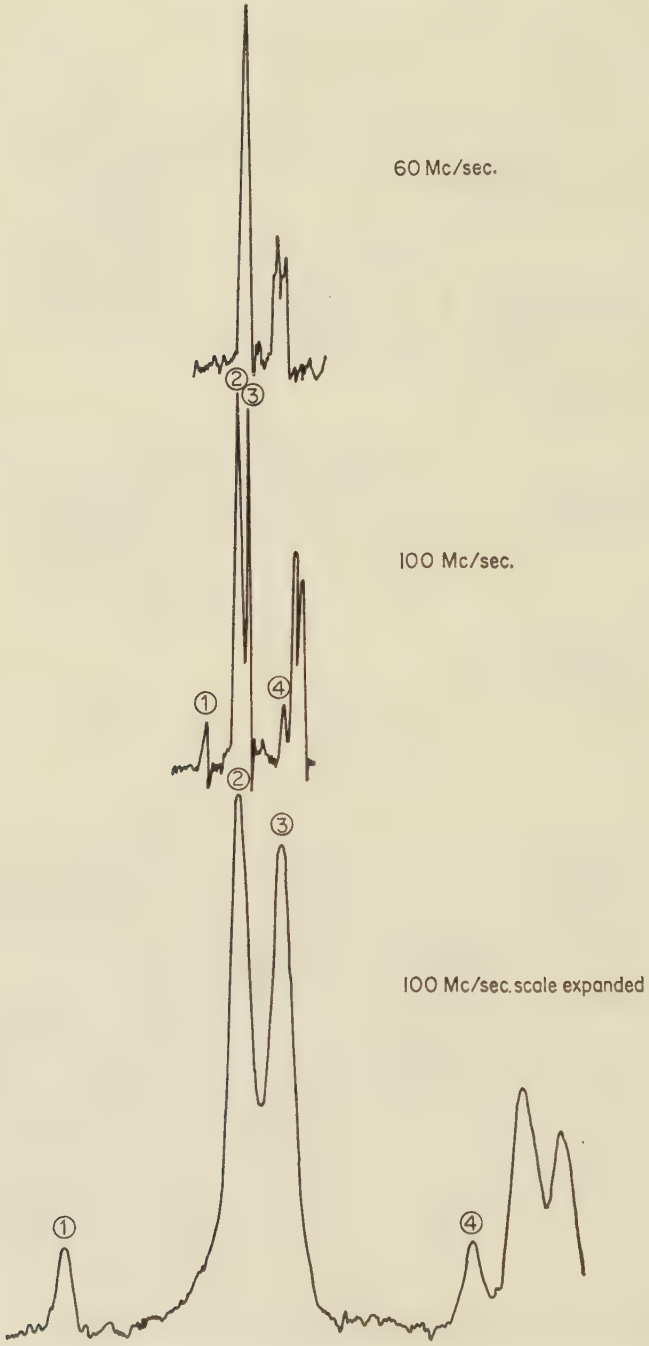


FIG. 14. The increased resolution obtained with a 100 Mc/s as compared with a 60 Mc/s spectrometer.

Varian Associates operating at 100 Mc/s. There are certain advantages with an instrument working at higher radio-frequency and higher field strength. Thus an increase in sensitivity is obtained and hence smaller samples are needed. Also, because a greater separation of lines of different chemical shift occurs, the available resolution is increased. An example of this greater resolution is shown in Fig. 14 where part of a spectrum run at 60 Mc/s and at 100 Mc/s is contrasted.

The use of super-conducting magnets for high resolution n.m.r. studies will enable even greater sensitivity and increased resolution to be reached.

Preparation of Samples

High resolution n.m.r. spectra are usually made with either pure liquid samples or, in the case of a solid material, with a solution of the substance in a suitable solvent. Sometimes a solvent may have absorption lines overlapping those of the sample and it may be necessary to obtain the sample spectra in two different solvents. Gaseous samples can be recorded but there are difficulties due to poor signal-to-noise ratio. When gaseous samples are examined it is under a pressure of several atmospheres.

With a liquid or solution, sufficient volume is required so that the sample tube is completely filled in the region of the sample coil. This usually means that the sample tube has to be filled to a depth of at least 3 cm (about 0·45 cm^3). When samples are filled to this minimum depth, care has to be taken that the tubes are not spun too quickly as the formation of a small vortex can severely affect the field homogeneity. Smaller volumes of material can be studied by inserting a plug in the bottom of the sample tube. The volume magnetic susceptibility of the plug and the solution must be roughly equal otherwise the field homogeneity will be adversely affected.

In general as concentrated a solution as possible should be examined. However, as a result of intermolecular interactions in solution, the chemical shifts of many lines in some solvents can be a function of concentration. In some extreme cases this can amount to several parts per million and will vary for different groups within the molecule. Another undesirable effect which can occur with concentrated samples is a broadening of the line indicating an apparent loss of resolving power. This effect can arise in viscous solutions as a result of incomplete averaging of nuclear dipolar interactions when the movement of the molecules is restricted. Line broadening may also occur in dilute solutions of nuclei when the resonating group is attached in a fairly rigid manner to a large molecule. An example of this is the signals from the olefinic protons to

steroids which are broad compared with the sharp peaks associated with nuclear methyl groups.

An impression of the sensitivity for detecting protons with a modern commercial instrument, such as the Perkin-Elmer R10, is that a single proton of approximately 0·02 M solution can be detected if it gives a single narrow line. A proton in a compound of molecular weight 250 can, therefore, be detected if 1·0 mg of sample is dissolved in 0·2 cm^3 of solvent. The use of a time-averaging computer device, see p. 41, can increase the sensitivity.

The samples should be free, as far as possible, of any small amounts of foreign matter as this can lower the resolution obtained if they drift into the region of the sample coil as the tube spins. To obtain the best separation in the spectrum, it is often important to remove dissolved oxygen from the sample. This is because the presence of oxygen molecules affect the spin–lattice relaxation processes, giving rise to broadening of the signals. Oxygen can be removed by distilling the sample in a vacuum or by repeatedly freezing and evacuating the sample. The concentration of impurities which can be allowed in the sample depends upon the way the lines from the impurity lie in the region of the spectrum under consideration. If the impurity has a much lower molecular weight than the test material, a small amount may give very strong lines in the spectrum, especially if the impurity contains many identical protons.

SOLVENTS

The solvent selected has to be one which does not produce signals in the region under examination or take part in associations with the solute molecules which can cause selective displacement of components. Suitable solvents used for n.m.r. work include deuterated chloroform, normal chloroform, carbon tetrachloride, carbon disulphide, methylene chloride, dimethyl sulphoxide, dioxan, pyridine and cyclohexane. The line positions of some solvents are given in Table 3.

REFERENCE MATERIALS

A reference line is usually included on each spectrum from which the chemical shifts of signals can be measured. The two methods which are used are:

(*a*) An external standard is placed in a sealed capillary tube which is then inserted into the sample tube. This avoids errors caused by displacement of the reference material resonance position due to possible intermolecular effects. However, in this case it is necessary to apply a correction factor to all line positions in order to compensate for

the difference in magnetic susceptibility of the standard and reference solutions.

(*b*) The second method is to add an internal standard directly to the sample. This method avoids the necessity for bulk susceptibility corrections but, of course, is open to the objections that the measurements can be influenced by the effects of molecular association between the reference material and the test sample. Tetramethylsilane is usually used and these molecular association effects are usually very small with this material. It has the additional advantage that its resonance line lies to

TABLE 3. Approximate Line Positions of some Protic Solvents
(The positions vary a little with solute)

Solvent	τ	Solvent	τ
$CF_3.CO_2H$	0·17	Dioxan	6·32
$H.CO.NH_2$	2·15 (CH)	$CH_3.OH$	6·53 (CH_3)
$CHCl_3$	2.73	$(CH_3)_2SO$	7·4
Benzene	2·73	$(CH_3)_2CO$	7·83
$CHBrCl_2$	2.80	$CH_3.CO_2H$	7·90 (CH_3)
$CHBr_3$	3·15	$CH_3.CN$	8·00
CH_2Cl_2	4·70	Cyclohexane	8·57
H_2O	*ca.* 5·2	$(CH_3)_3OH$	8·73
$CH_3.NO_2$	5·67	Pyridine	1·50–3·10

a higher field than almost all other signals so that chemical shifts of most compounds, when measured with respect to it, are of the same sign. The tetramethylsilane can be added to each bottle of solvent used. A concentration of about 0·2% is suitable for most purposes.

For solutions in H_2O and D_2O, dioxan (τ 6·32) and acetonitrile (τ 8·00) are good internal standards, better than *t*-butanol, and DSS ($Me_3Si[CH_2]_3.SO_3Na$) with τ 10·00 is highly convenient.

SAMPLE TUBES

It is usual to use cylindrical sample tubes because these are easy to fill and to use. They are about 15 cm in length. It is worth noting that different n.m.r. instruments use slightly different outside diameter tubes. Those used in the Varian instruments are 5 mm outside diameter, whilst those used with Perkin-Elmer instruments are 4·6 mm diameter. The use of cylindrical sample containers have some disadvantages. A considerable volume of the sample is unused with these tubes because the radio-frequency coil is much shorter than the liquid column. Also if an external reference sample is used in a central or annular capillary, the chemical shift values have to be corrected for the difference of susceptibilities of the two liquids. The first disadvantage can be overcome by

using a block made of plastic material such as nylon in the glass tube. Other types of sample container which have been tried are spherical sample holders or spherical samples, and methods have been described for preparing spherical samples which appear to be useful when only small quantities are available. This can give a good signal-to-noise ratio with much less material than is required with the normal cylindrical sample tube.

Operation of Instrument

It is possible with n.m.r. instruments to obtain either absorption or dispersion signals (see Fig. 15). However, with nuclei possessing a quadrupole moment the signals are broad and it can be difficult to

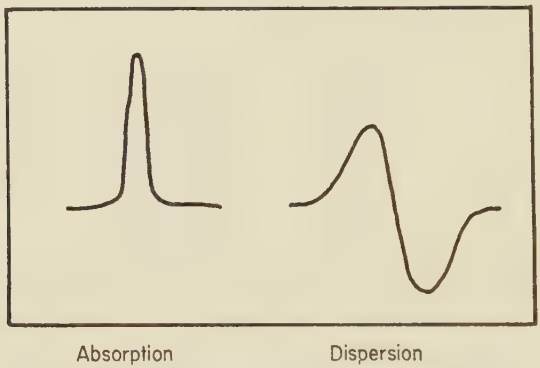


FIG. 15. The absorption and dispersion signal.

determine the band centre using the absorption signal. In these cases the dispersion signal can be useful. In most cases of interest to the organic chemist it is the absorption signal which is recorded.

The precise details for setting up the n.m.r. instrument will vary depending upon the particular instrument and will also vary considerably from an electro-magnet to a permanent-magnet type. Manufacturer's manuals should therefore be consulted for these details. We shall only discuss some of the more general aspects likely to be met by the organic chemist.

It is important to have a routine method of testing for resolution, reproducibility and to ensure that the instrument is performing satisfactorily. The n.m.r. spectrum of acetaldehyde is often used to provide this rapid check. Acetaldehyde is useful because it has a high vapour pressure enabling easy purification, low viscosity in the liquid phase, giving long relaxation times and narrow line widths, no broadening due to exchange of protons, and above 1000 G, the second-order splitting

is negligible. Vacuum distillation of the sample is required as paramagnetic broadening due to oxygen can occur if a true test of magnet homogeneity is required. The spin coupling constant is 2·85 c/s. The spectrum of the CHO group of acetaldehyde is shown in Fig. 16. The

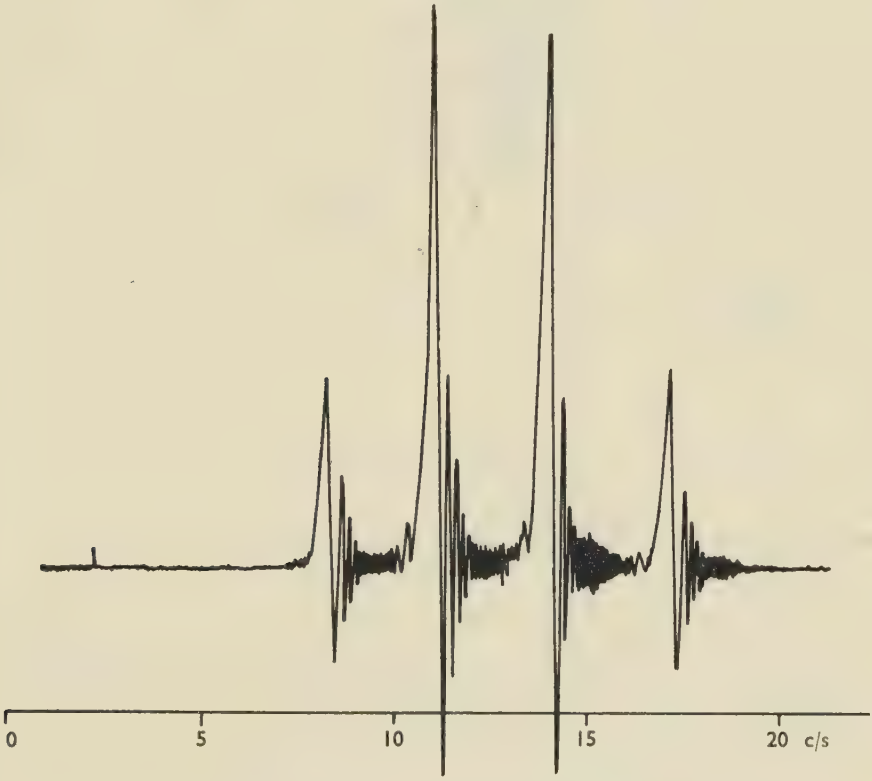


FIG. 16. Spectrum of the CHO group of acetaldehyde.

homogeneity of the magnet is checked by examining the half-height line width. If this is 0·6 c/s, or less, the resolution is equivalent to 1 in 10^8 or better at 14,092 G.

Factors Determining the Quality of a Spectrum

There are a number of factors which can affect the quality of an n.m.r. spectrum. We shall summarize some of these important factors. We have illustrated some of the effects using the CHO spectrum of acetaldehyde.

(a) Poor homogeneity of the magnet. This can be improved by adjustment of shim coils or by additional precycling.

(*b*) Incorrect, or lack of, spinning of sample tube. This can be caused by having the sample tube in a faulty position in the turbine. The resultant loss in resolution is shown in Fig. 17.

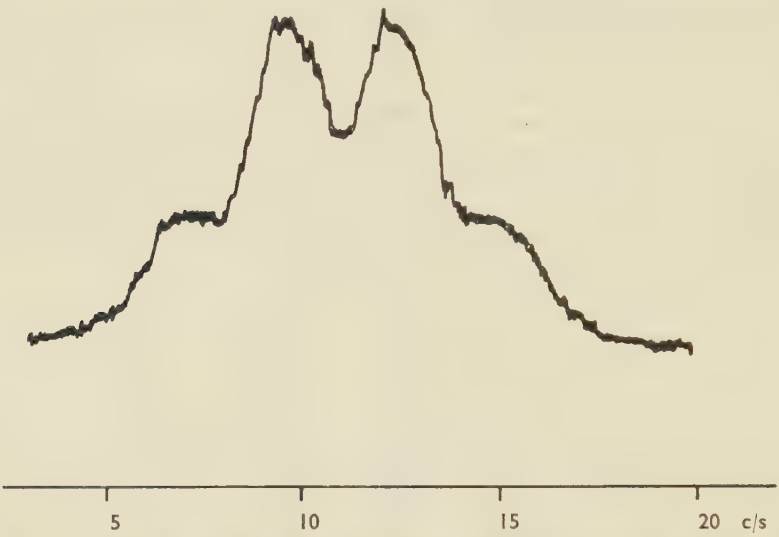


FIG. 17. The loss in resolution of spectrum of acetaldehyde due to lack of spinning. (Other conditions were the same as for previous figure.)

(*c*) Increased R.F. power. If too much R.F. power is delivered to the nuclei, saturation of the spin system can occur. This causes a broadening of the signal and a reduction in the peak height occurs as the R.F. level height is increased. This is illustrated in Fig. 18.

(*d*) Incorrect time constant of recorder. If the time constant is too long, distortion and line broadening can occur as shown in Fig. 19.

(*e*) Incorrect field sweep. If the field sweep is too rapid, fine structure may not be resolved and some displacement of line position may occur.

(*f*) Sample effects. A known optimum concentration of sample leading to effects on viscosity, or the presence of paramagnetic ions, can cause broadening of the signals.

Scale Expansion

It is possible, having obtained the full spectrum of the molecules under consideration, to select a portion of the spectrum for some detailed study on an expanded scale. This is carried out by using a scale factor control which reduces the amplitude of the full sweep, and expands the horizontal co-ordination of the spectrum. The full sweep usually commences

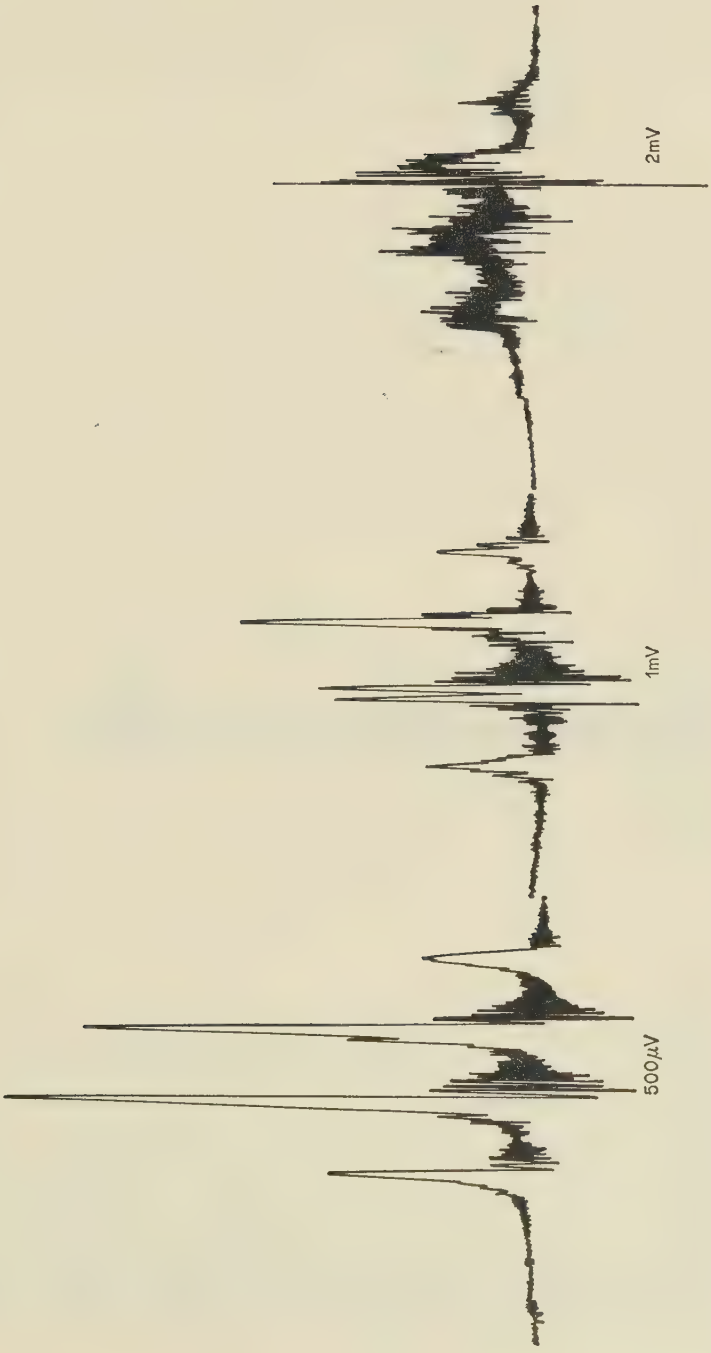


FIG. 18. The loss of resolution due to use of too much R.F. power.

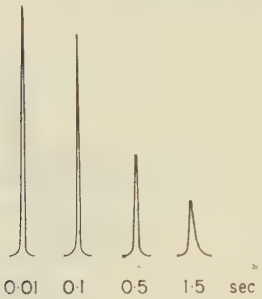


FIG. 19. Distortion of signal due to use of incorrect time constant.

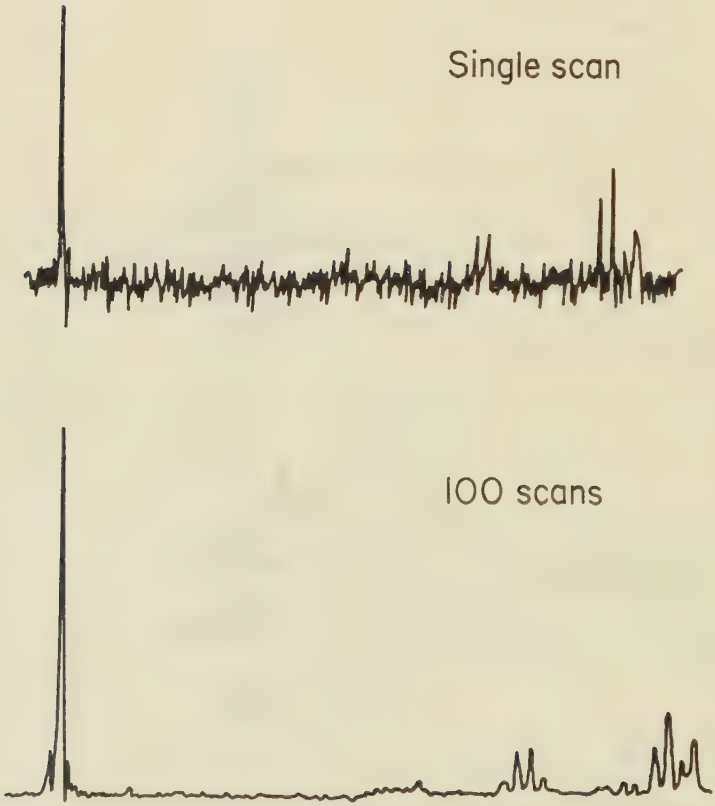


FIG. 20. The improvement in the signal-to-noise factor in ethyl benzene when scanned and summed 100 times by the Varian time-averaging computer (after Varian).

from a zero position on the precalibrated charge and not the centre point of the spectrum. Changing the scale factor may involve changing the field shift controls and adjustments of R.F. level, time constant, recorder sensitivity, and chart speed may become necessary.

Time-Averaging Computer

Recently a time-averaging computer device has been introduced. This receives the spectrometer signal and the signal information is added over a number of spectral sweeps. Whilst the signal information adds directly, the noise is the square root of the number of scans. Thus an increase in signal to noise can be obtained equal to the square root of the number of scans. Coherent noise can also be averaged which is not synchronous with the sweep rate. This enables the spectrum of other dilute solutions to be made and, one can obtain by scanning 100 times, a factor of 10 enhancement of the signal-to-noise ratio. An example of an improvement in the signal-to-noise factor is shown in Fig. 20.

Measurement of Chemical Shift

The chemical shifts of a compound can usually be read, with sufficient precision, directly from the precalibrated charts provided. In this case the maximum instrument error may be of the order of 1 c/s. The error can be reduced by using a smaller scale factor so that the chemical shift of nuclei which lie close to a reference material can be measured with more accuracy. Greater precision can be obtained, if necessary, by using an external audio-oscillator to modulate the R.F. source. This produces side bands on the spectrum of a separation of a definite number of cycles. Frequency accuracy to about 0·01% is then possible.

Integration

The integrating devices give a stepped output in which the step heights are proportional to the number of nuclei beneath the corresponding signal. This is shown in Fig. 21a and b.

Errors in integration can arise if there is saturation of the nuclear resonance signal, or if the dispersion mode is not completely excluded. These can be eliminated by using a rapid field sweep, and by careful adjustment of the phase detector controls. If saturation is suspected, the R.F. power can be lowered.

The accuracy of the method depends mainly on the concentration of the material investigated and the number of protons present. The correct and incorrect appearance of the integral trace is shown in Fig. 21b.

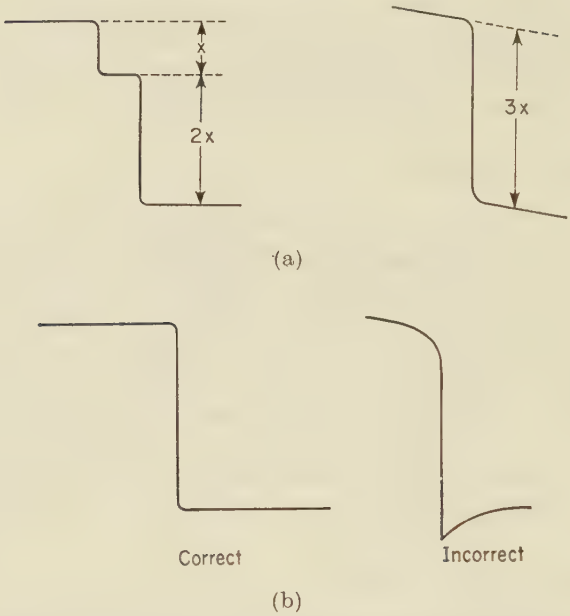


FIG. 21. (a) The integrated trace showing the way in which the step heights are proportional to the number of nuclei.
(b) Correct and incorrect appearance of the integral trace.

Double Resonance (Spin Decoupling)

An important technique which is useful for simplifying a complex spectrum is the technique of double irradiation. The aim of the technique is to remove the effect of spin coupling by applying a second R.F. field in addition to the one used for observation. The method consists of disturbing one group of nuclei with a strong R.F. field close to their resonance frequency. This leads to saturation and effectively decouples them from the remaining nuclei. The spectrum is simplified as a result of the spin decoupling and the chemical shift of groups which are hidden by unrelated absorption can be revealed. The relative signs of coupling constants may also be determined.

Commercial n.m.r. instruments provide an accessory to enable spin decoupling experiments to be made. In simple spectra where groups are well separated, a field sweep technique can be used. Two R. F. frequencies are used at a known separation with normal field sweep. To observe a more extensive spectrum while a particular group is saturated, a frequency sweep technique is used. In this case the spectrum is swept repeatedly while the saturating frequency is changed after each sweep.

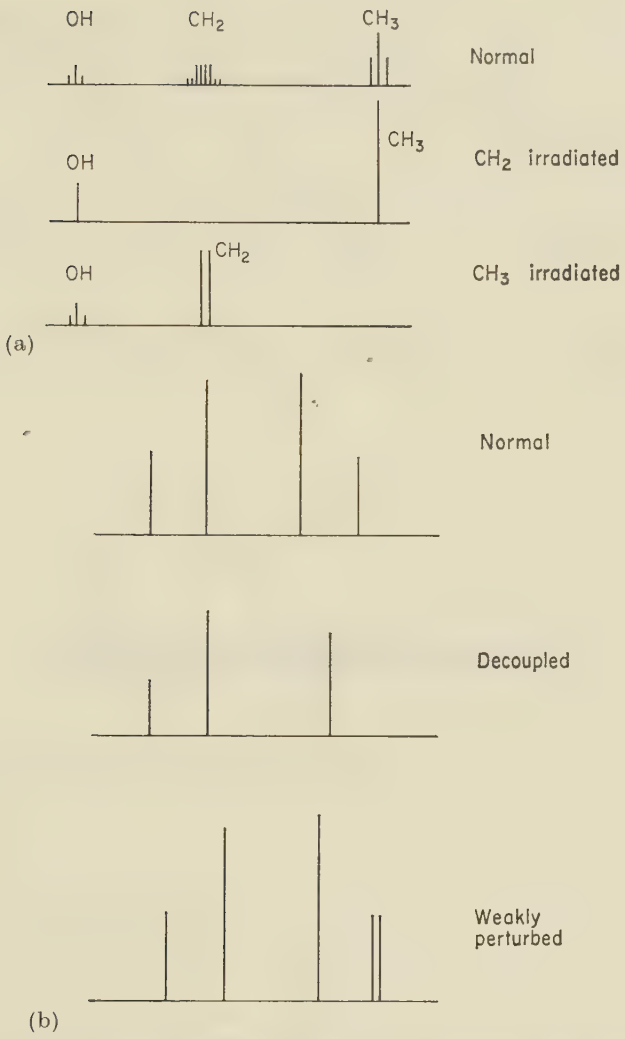


FIG. 22. Spin decoupling effects. (a) Ethyl alcohol showing the effect of irradiation of the CH_2 group and of the CH_3 group. (b) 2-Bromo-5-chlorothiophene showing the effect of irradiation on one component of the AB system $J_{AB} = 4$ c/s producing decoupling and also of weakly perturbing the system.

Poor spinning of the sample can cause difficulties in the effectiveness of the spin decoupling. Some examples of the use of the spin decoupling technique are shown in Fig. 22.

Relaxation Measurements

We have indicated earlier, page 21, that there are two relaxation times, the spin–lattice T_1, and spin–spin T_2. Methods have recently been

described which enable measurements of these parameters, either without modification or with only slight modification, to commercial high resolution n.m.r. spectrometers. Full details of the experimental methods are given in the references.[12,13] Here we shall only outline the basis of these measurements.

The relaxation time T_2 can be determined from the full line width at half height. If, however, T_2 is very long (> 5 sec), the line width is determined by the magnet inhomogeneity. With a Varian A-60 instrument relaxation times having values up to about 500 msec can be measured satisfactorily.

T_1 values can be determined either by the "direct method" or by the method of "progressive saturation". In the direct method the sample is

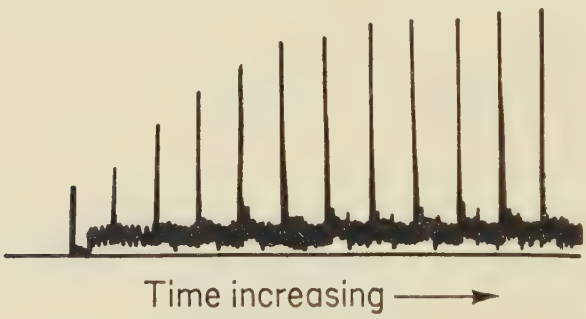


FIG. 23. Appearance of oscilloscope trace showing the recovery of the amplitude of a single n.m.r. line following complete saturation with a time constant essentially T_1.

saturated by application of a strong R.F. field. When the R.F. field is suddenly reduced to a non-saturating value, the n.m.r. signal recovers exponentially with a time constant which is essentially T_1 (see Fig. 23). The method is best suited for relaxation times between 50 msec and 25 sec. In the second method the relaxation time obtained by progressive saturation of the signal is the geometric average $\sqrt{T_1 T_2}$. There are two main ways of carrying this out. These are measurement of peak height, or of area as a function of the amplitude H_1 of the R.F. field. This method is best used as a relative method and is not as reproducible as the "direct method". Pulse methods are also used.

Quantitative Analysis

The high resolution n.m.r. spectrometer is of considerable use as a qualitative tool to enable an unknown substance to be identified. It is also useful for quantitative studies. The fact that the area of an n.m.r.

peak is directly proportional to the number of nuclei involved can be most valuable. For analytical purposes it is sufficient to find a resolved peak for each of $n-1$ components in an n component mixture, and to know how many nuclei per molecule are represented by each peak.

An example of this is the analysis of a hydrocarbon mixture of, say, tetralin, naphthalene and hexane. By integrating separately the aromatics, α-hydrogens and β-hydrogens, plus aliphatics, it is possible to set up a series of three simultaneous equations whose solution can be solved for the mole fractions for the three components.

Integration can also be particularly useful for the analysis of tautomeric mixtures of keto and enol forms. The advantage of the n.m.r. technique is that, unlike titration methods, the equilibrium is not disturbed during the measurement.

If the compound is pure, the various multiplets resulting from chemical shifts and spin coupling bear a relationship with each other so that the ratios of the integrated intensities are ratios of integers. Hence, if a peak in a spectrum can be identified with, say a methyl group, then the total number of protons in a complex organic molecule can be determined. An example of this is proton counting in a steroid 3-acetoxypregnane-20-one where the hydrogen on C-3 is observed as a separate peak and taken as one proton. The integral of the remaining absorption shows this to be associated with 35 protons. Hence, there are 36 protons in the sample consistent with the empirical formula $C_{23}H_{36}O_3$. Further uses of integration for the determination of the structure of unknown molecules are given in the examples later in the book.

Another use of quantitative analysis is for the determination of the total amount of an element present. Thus, by comparing the total integrated intensities of the entire spectrum in sample tubes of identical cross-sectional area, it is possible to determine the percentage of some element, say hydrogen, in an unknown sample. The method is rapid, non-destructive and compares well with results obtained by the standard combustion method.

For best quantitative results, spectra are run at as high a field as possible to take advantage of increased resolving power and sensitivity, thin-walled sample tubes with good filling factor are used, and care is taken in adjusting the integral trace.

5. Hydrogen Bonding

Nuclear magnetic resonance measurements provide a new technique for the study of hydrogen bonding and other molecular interactions. This led directly from the observation that the chemical shift of the proton signal of the ethanol OH group was temperature dependent. The method is thought to be superior in sensitivity to frequency shift measurements using infra-red spectroscopy although, in fact, infra-red spectroscopic intensity measurements can compare more favourably in sensitivity. For strong hydrogen bonds the information obtained is largely complementary to that obtained from infra-red absorption measurements. The chemical shift of the hydrogen signal for the non-associated state is obtained either by successively diluting with an inert solvent and extrapolating the results to infinite dilution, or by direct measurement in a gaseous condition at high enough temperatures to ensure complete dissociation. The n.m.r. signals are usually disposed to a lower field by the formation of hydrogen bonds. Exceptions to this behaviour have been connected with association to certain atomatic molecules.

This shift to low fields on hydrogen bond formation can be explained by assuming that the purpose of group Y is to provide a strong electric field in the neighbourhood of the XH bond. This field will tend to draw the proton away from the bonding electrons, thereby reducing the electron density immediately around it. The diamagnetic circulation within the hydrogen atom will also be inhibited by the presence of a strong electric field. The magnetic field effects on the proton in XH, due to the current induced in the Y atom, can also provide a net contribution to the proton chemical shift.

Among the many studies of hydrogen bonding are the studies of the simple alcohols. Using the solvent dilution method, the hydroxyl proton of ethyl alcohol can be observed to move to a higher field than the signal of the methyl group. Some n.m.r. spectra taken at various dilutions are shown in Fig. 24. The chemical shifts of phenols are also affected by concentration of solvents and temperature. The n.m.r. spectra of carboxyl shifts in non-polar solvents are different from those observed with alcohols and phenols in that the carboxyl proton lines are invariant with concentration. This is because of the tendency of the carboxylic

acids to form suitable dimers. Intermolecular hydrogen bonding gives a variation of chemical shift with change of temperature or concentration, intramolecular hydrogen bonding gives a variation of chemical shift only with a change of temperature.

Because of the great variation of the chemical shift of protons in various types of OH groups, it is often not possible to identify their signals in the spectrum of a complex molecule. The signal from this group may also be assigned to other structural features. This uncertainty

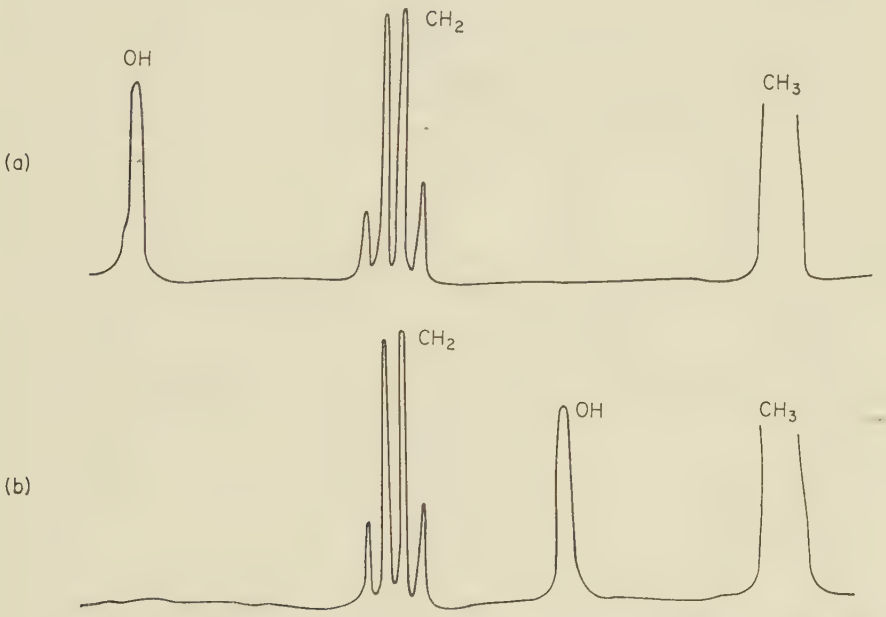


FIG. 24. Nuclear magnetic resonance spectra (a) of liquid ethyl alcohol and (b) a dilute solution in $CHCl_3$ showing the shift of the OH resonance.

in the assignment of the OH proton may be overcome by variation of temperature or concentration, or by shaking the sample containing the hydrogen group with deuterium oxide, thereby replacing the hydrogen atom by deuterium.

When a hydrogen atom is attached to nitrogen, because of the electric quadrupole moment of the ^{14}N nucleus, various types of behaviour are observed. Thus, the single sharp lines, broad lines, or triplets are noticed. The triplet is observed with rigorously purified ammonia and some amines in acid solution, and arises from the spin–spin coupling in the nitrogen nucleus. Many amines, however, give rise to a very broad band which has been associated with the nitrogen quadrupole moment

affecting the spin–lattice relaxation time. Free amines give rise to a sharp observation line which is associated with rapid chemical exchange of the amino hydrogen atoms. This exchange is inhibited by protonation of the amine and is dependent upon the pH of the solution. See Table 12 for observations on the chemical shift position and appearance of compounds such as alcohols, amines, thiols, amides and acids which can be affected by hydrogen bonding.

6. Isotopes other than ^1H

Fluorine (^{19}F)

The fluorine nucleus ^{19}F has $I = \frac{1}{2}$ and the resonance frequency of the fluorine nucleus is a little lower than that of hydrogen (56·5 Mc/s in a field of 14,100 G) and fluorine resonance absorption can be readily examined merely by using a different R.F. source and amplifier. The line positions of fluorine spectra appear to be very sensitive to the choice of solvents.

Correlations for fluorine groups are given in Tables 35 and 36.

Phosphorus (^{31}P)

The stable isotope of phosphorus is ^{31}P which has a spin of $\frac{1}{2}$. The resonance frequency is less than that for the proton, about 17·2 Mc/s in a magnetic field of 10,000 G, and 24·3 Mc/s at a field of 14,092 G, and a separate probe is required as well as R.F. amplifier source and bridge controls. Unfortunately, the signal strength of the phosphorus resonance, because of its smaller magnetic moment, is only some 7% of that of the ^1H or ^{19}F nuclei at the same field strength. However, the chemical shifts cover a range of 500 p.p.m. compared with about 10 p.p.m. for ^1H resonance and therefore overlapping of peaks is less important with phosphorus and a lower signal-to-noise ratio is acceptable. Lower resolution can be tolerated and sample tubes of larger diameter may be used and non-spinning conditions apply. The samples commonly examined nevertheless had to have been of high concentration, at least 1 M in phosphorus. This limits its usefulness to solid samples. The reference material frequently used in 85% aqueous phosphoric acid which is used as an external standard. Recently a technique has been described for measuring the chemical shifts of weak spectra containing broad resonance peaks. In this way, adenosine di- and tri-phosphate in 0·09 M solutions were examined, and it was suggested that the method might be capable of use with solutions as dilute as 0·01 M.

The spin coupling constant for compounds with a hydrogen or fluorine atom directly attached is very large (some 500–700 c/s for hydrogen atoms); for compounds with one or two other atoms separating the phosphorus and the proton, the splitting is much smaller. However, with $P(OMe)_3$ eight of the ten expected lines can be resolved.

Correlations for phosphorus groups are given in Table 37.

Nitrogen (^{14}N)

The nitrogen nucleus possesses a quadrupole moment ($I = 1$) and, therefore, signals are broad. Chemical shifts have, however, been observed for the ^{14}N nucleus in various molecular environments. When a proton is bonded to a nitrogen atom, the proton signals are often broad and sometimes the signal is hardly detectable. This occurs because the quadrupole moment of the nitrogen nucleus gives rise to a strong relaxation mechanism. A proton attached to a nitrogen atom gives rise to three lines due to the spin–spin splitting of the ^{14}N ($I = 1$). Broadening of the signal can sometimes be reduced by double-irradiation experiments.

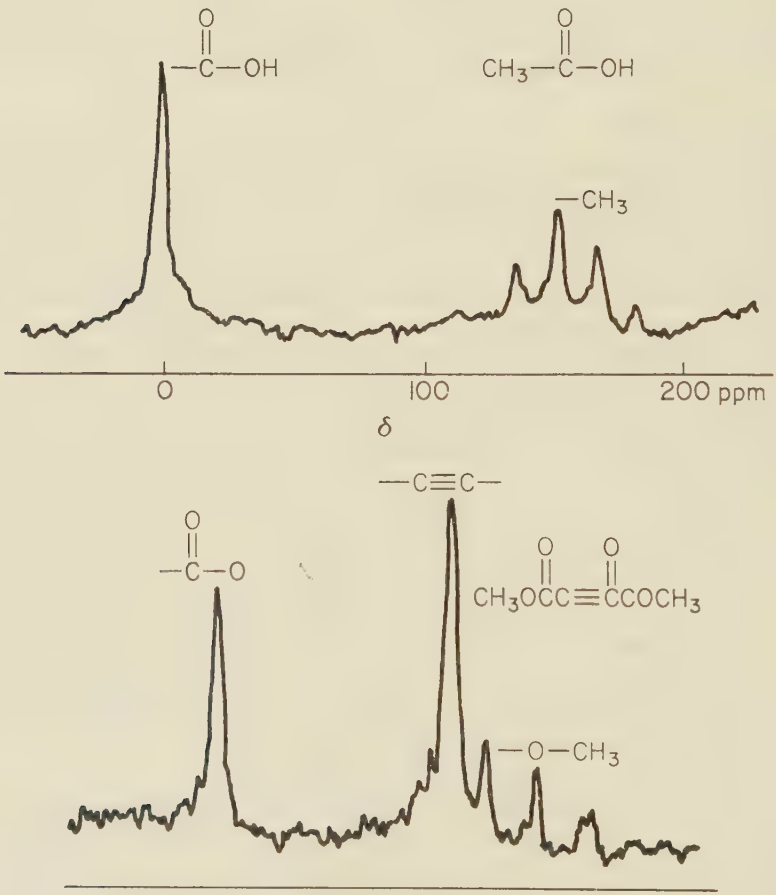


FIG. 25. A ^{13}C resonance spectrum of acetic acid (above) and dimethyl acetylene dicarboxylate (after Lauterbur, P. C., *Ann. N.Y. Acad. Sci.* **70**, 841, 1958).

Carbon (^{13}C)

Although the natural abundance of ^{13}C is only 1·1%, the exciting possibility of obtaining high-resolution spectra corresponding to the ^{13}C nuclei has been studied. This means that direct information on carbon atoms, which are not attached to hydrogen atoms, such as carbonyl groups, is possible. The ^{13}C isotope has a spin of $\frac{1}{2}$. A technique has been developed, using dispersion signals recorded with sweep rates of the order of 100 c/min which enables the detection of signals from compounds with molecular weights up to 400. This work was carried out with a Varian high-resolution n.m.r. spectrometer operating at a frequency of 8·5 Mc/s. The resonant field at this frequency is about 7940 G. For accurate calibration a sample of methyl iodide enriched to 60% ^{13}C is used and the absorption mode is employed. The arbitrary zero of reference for most of the ^{13}C shifts obtained is the resonance of the carboxyl carbon in acetic acid.

A typical ^{13}C resonance spectrum of acetic acid is shown in Fig. 25. The larger peak arises from the carbon in the carboxyl group, whilst the four smaller peaks arise from the methyl carbon resonance. The spin–spin interaction with the three methyl protons splits the methyl carbon resonance into four components. There is no observable coupling of either the methyl or the hydroxyl protons with the carboxyl carbon.

Some correlations of ^{13}C chemical shifts are given on page 107.

7. Interpretation of a Spectrum

It is important to realize that, due to the rapid development of n.m.r. spectrometers, the n.m.r. spectra published in the literature may often be dissimilar, depending upon the particular radio-frequency field at which they have been recorded. Thus, in the literature, spectra are given which have been recorded at 30, 40, 60 and, more recently, 100 Mc/s. The change in the spectra arises from the difference in the origin of the chemical shift and spin coupling effects. Whilst the chemical shift between nuclei measured in parts per million remains constant, the spin–spin interaction between the nuclei is constant only in cycles/sec. Thus the spin–spin multiplets of chemically shifted groups tend to have greater overlap when recorded at low values of the magnetic field H_0 than at high values. A comparison of the n.m.r. spectra of a compound taken at two different operating frequencies showing the increased detail is shown in Fig. 14.

The first step in the analysis of an n.m.r. spectrum is to determine whether the lines close to each other are caused by chemical shifts or by spin–spin interaction. The spin–spin multiplicity can often be recognized from the patterns shown on pages 14, 16 and reference 11. In difficult cases, by obtaining the spectrum at a different field strength, it can be readily determined whether the line arises from chemical shift or spin coupling effect. Since the coupling constant is field independent, spin–spin multiplets will retain the same separation at a different field. Since the chemical shift is field dependent, the spacing between chemically shifted lines will vary as the field changes. Obtaining the spectrum in different solvents can also aid in the interpretation of complex patterns. Spin decoupling can also be of value in simplifying complicated spectra.

Once the distinction between spin–spin multiplets and chemical shift has been made, the chemical shift values can be determined for each line in the spectrum. The lines can then be assigned to specific proton groupings on the basis of their chemical shift and intensity. An analysis of spin–spin interaction can then allow conclusions to be drawn about spatial relationships of spin coupling nuclei. Intensity measurements of the peaks within the spectrum are often of value and can allow cross checks on assignments and sometimes even eliminate the need for

detailed assignments. If the molecule has a distinctive grouping containing a known number of protons, the peak for this grouping can serve as an internal calibration for the rest of the pattern. Some examples of varying complexity of the interpretation of various n.m.r. spectra, using chemical shift, spin coupling and integration, are given in the following pages.

Examples

EXAMPLE 1

The n.m.r. spectrum of a compound C_3H_6BrCl was run at 60 Mc/s and integrated (integral trace is shown) (Fig. 26). As can be seen, the spectrum consists of two groups of lines; a quintet $8-7{\cdot}5\tau$ and six lines

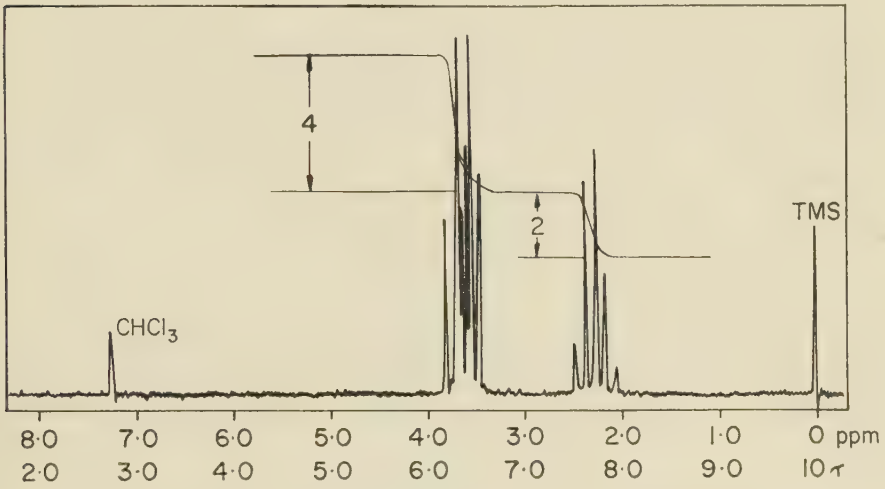


FIG. 26. The n.m.r. spectrum of C_3H_6BrCl.

at $6{\cdot}15$–$6{\cdot}55\tau$. The groups of lines integrate as two and four protons respectively. Now for two protons to give rise to a quintet they must have been equivalently coupled to four other protons, and the four other protons must be coupled to the first two protons, giving rise to two triplets, i.e. six lines. So we have group $—CH_2{\cdot}CH_2{\cdot}CH_2—$

$$\begin{array}{cccccc} & & 1 & 2 & 3 & \\ X— & CH_2— & CH_2— & CH_2— & X_1 \\ & & \downarrow & \downarrow & \downarrow & \\ & & t & q & t & \end{array}$$

The triplets overlap, but they can be sorted out from the fact that the coupling constant for the first order system is 6·5 c/s. So we have

methylene groups
- (2) give a quintet at 7·72τ
- (1) give a triplet at 6·30τ
- (3) give a triplet at 6·45τ

The compound is $ClCH_2CH_2CH_2Br$, and from correlation tables, X is Cl and X_1 is Br.

EXAMPLE 2

The fully integrated spectrum of compound I (C_9H_6SO, from analysis, mass-spectrum or unambiguous synthesis), was run in deuterochloroform at 60 Mc/s (Fig. 27).

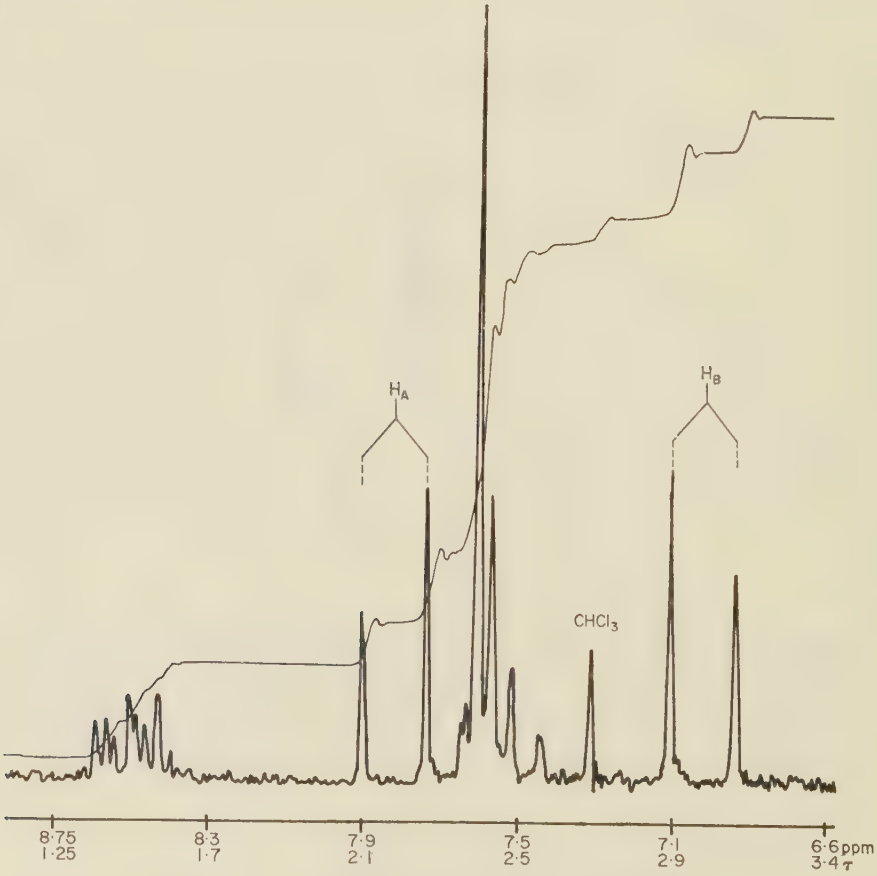
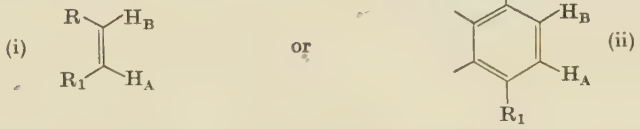


FIG. 27. The n.m.r. spectrum of compound C_9H_6SO.

The following signals were recorded, the integrator giving the intensity of the signals:

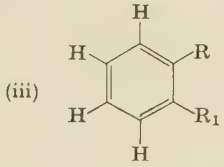
1—H (multiplet) at 1·47τ
1—H (doublet) at 2·20τ
3—H (multiplet) at 2·40τ
1—H (doublet) at 3·05τ

The signals at 2·20 and 3·05τ make up an AB quartet with a coupling constant of 6·7 c/s. This information leads to the structural feature (i), or (ii)

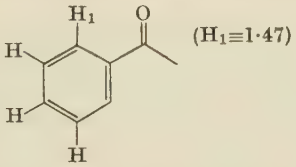


where R is any strong electron-withdrawing group.

The group of protons at 2·40τ are aromatic and coupled to the proton at 1·47τ (*o*, *p* and *m* coupling is discernible). This information leads to the structural feature (iii)

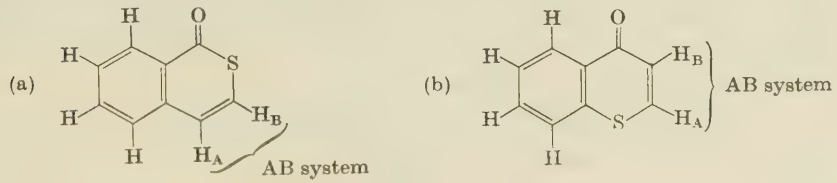


Now since one proton is at 1·47τ and part of this aromatic nucleus, it must be *ortho* to a very strongly deshielding group, i.e.

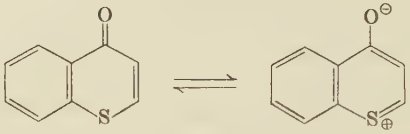


The AB quartet arises from another portion of the molecule.

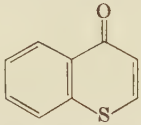
Two rings are present from the molecular formula, so one is compelled to write two structures (a) and (b)



From correlation tables the structure (b) fits the observed chemical shift of 3·05τ of the proton H_B better than structure (a). No information is available for proton H_A but structure (b) being potentially completely aromatic, i.e.



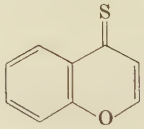
would appear to be more apt for the assignment of this proton. The n.m.r. spectrum does not lead unequivocally to the structure (b) as being correct but, in conjunction with the u.v. spectrum and i.r. carbonyl absorption, the structure is



because it exhibits absorption at 1665 cm^{-1} in the i.r. spectrum.

(Ar—CO— = *1665 cm^{-1}*
Ar—CO—S— = 1720 cm^{-1}
C=S 1200 – 1050 cm^{-1})

Another possibility is (iv) which could not be eliminated on any

(iv) 

a priori assumptions about correlations between observed and tabulated τ values, but the i.r. spectrum will establish (iv) as being the wrong compound. The proton in a peri position to a thiocarbonyl group is usually more deshielded than that peri to a carbonyl group (0·27τ).

EXAMPLE 3

The spectrum of the compound $C_{10}H_{13}NO_2$ was recorded in $CDCl_3$ at 60 Mc/s on a Varian A-60 spectrometer (see Fig. 28). The integral trace (not shown), reveals the following features along with the measured chemical shifts. It has been assumed that the lines at 3·17 and 2·59τ constitute an AB quartet and the chemical shifts were calculated from the equality, $\nu_3-\nu_4=\nu_1-\nu_2=J_{AB}$:

$$(\nu_1-\nu_3) \equiv (\nu_2-\nu_4) = \sqrt{(\delta_B-\delta_A)^2+J_{AB}^2}$$

therefore $\delta_B-\delta_A$ is calculated (see page 13).

The midpoint of the quartet being 0, enables δ_A and δ_B to be found by adding and subtracting $\frac{1}{2}(\delta_B - \delta_A)$ to and from 0.

3 protons at 8·62 (triplet) midpoint gives τ value

3 protons at 7·88 (singlet)

2 protons at 6·00 (quartet) midpoint gives τ value

2 protons at 3·17 (B doublet) } C.G. of doublets as calculated
2 protons at 2·59 (A doublet) } above gives τ values

1 proton at 2·09 (broad)

The integral trace shows thirteen protons, thus confirming the hydrogen analysis of $C_{10}H_{13}NO_2$.

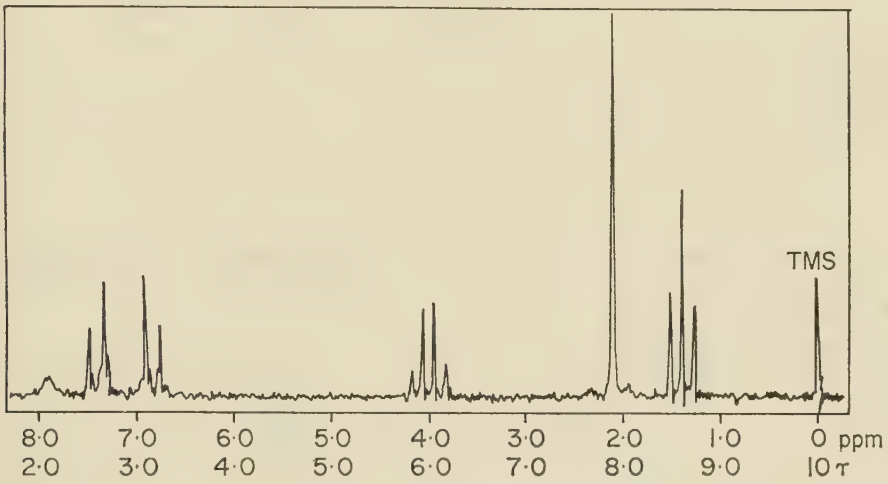
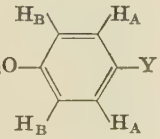


FIG. 28. The n.m.r. spectrum of $C_{10}H_{13}NO_2$.

Three protons at 8·62τ are coupled to two protons at 6·00τ by 7 c/s. This is a typical feature to be associated with an ethyl group, $—CH_2—CH_3$. From correlation tables, for the group $X—CH_2CH_3$, X is found to give the best agreement with the observed τ values if it is —OPh. (The calculated values are $—CH_2 = 6·10$; $—CH_3 = 8·63\tau$.)

The AB quartet is of double intensity, and made up from four aromatic protons in pairs being in equivalent chemical environments. The structure deduced so far is (I):

J_{AB} = 8 c/s

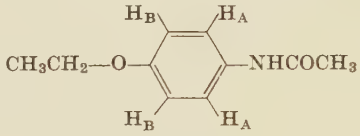


(I) C_8H_9O Y = C_2H_4NO

Three of the hydrogens in Y are part of a methyl group (7·88τ singlet) which is not attached to nitrogen. From correlation tables CH_3CO—NHR 7·98τ, and —NH (broad 1·5–5τ). The most reasonable procedure now is to calculate from correlation tables the expected τ values of the four aromatic protons and compare these with those observed.

Position	*o*	*m*	*p*	
Relative to 2·73 (PhH)	0·2	0·2	0·2 ...	—OEt
	−0·4	0·2	0·3 ...	—NHCOR
	−0·5	−0·2	−0·2 ...	—CONHR

Now if as deduced so far $C_{10}H_{13}NO_2$ is (II):



(II)

$$H_B \text{ is } 2{\cdot}73 + 0{\cdot}2_o + 0{\cdot}2_m = 3{\cdot}13 \text{ (observed } 3{\cdot}17)$$

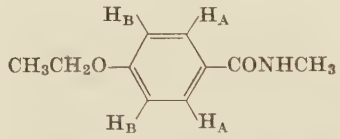
$$H_A \text{ is } 2{\cdot}73 + 0{\cdot}2_m - 0{\cdot}4_o = 2{\cdot}53 \text{ (observed } 2{\cdot}59)$$

This agreement is very good considering that these correlations when used additively as shown cannot be expected to give more than a rough agreement (0·1 p.p.m).

If the compound were (III), then

$$H_B \text{ is } 2{\cdot}73 + 0{\cdot}2_o - 0{\cdot}2_m = 2{\cdot}73$$

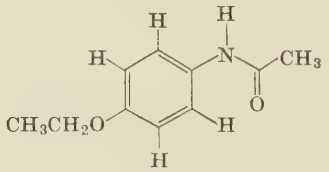
$$H_A \text{ is } 2{\cdot}73 + 0{\cdot}2_m - 0{\cdot}5_o = 2{\cdot}43$$



(III)

which is not correct, apart from the wrong chemical shift for the methyl group in part Y.

The structure of $C_{10}H_{13}NO_2$ is therefore



Phenacetin

EXAMPLE 4

A compound C_7H_7N exhibited the following features in its n.m.r. spectrum run at 60 Mc/s in $CDCl_3$ (Fig. 29):

2 protons at 1·48τ (doublet)
2 protons at 2·78τ (doublet)
1 proton at 3·38τ (quartet)
1 proton at 4·10τ (quintet)
1 proton at 4·60τ (quintet)

The low field doublets at 1·48 and 2·78τ are coupled to one another by 6·0 c/s, thus an AB quartet of double intensity is indicated. Correlation

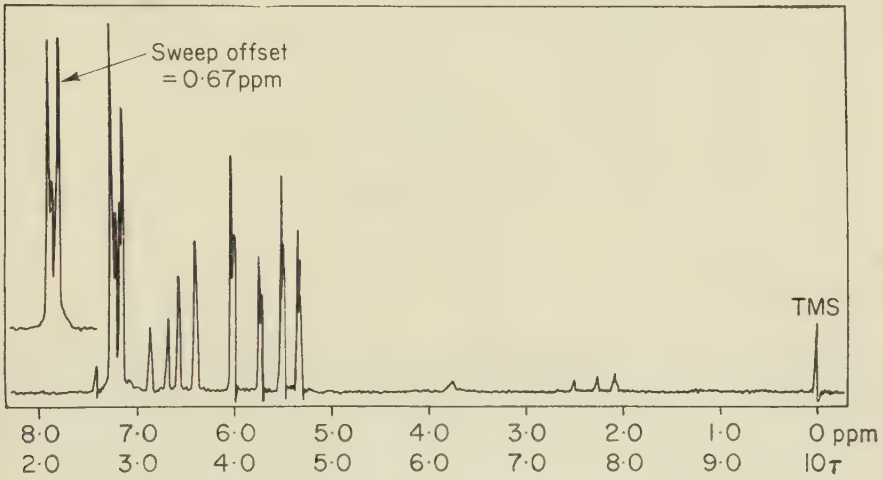
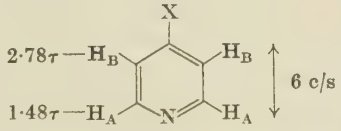


FIG. 29. The n.m.r. spectrum of C_7H_7N.

tables indicate that a proton at 1·48τ could be at the α-position of a pyridine ring (1·50τ). This is substantiated by the fact that no NH protons or n-Alkyl groups are discernible in the spectrum. The coupling constant of 6 c/s corresponds to 2,3 coupling, and leads one to write the part structure I.

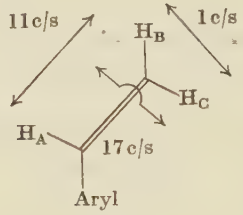
I



where X = C_2H_3 (3,5 coupling of about 2·0 c/s is also discernible).

The group X contains three olefinic protons. A quartet at 3·38τ indicates that this proton is coupled to two non-equivalent protons. The coupling constants involved are 11 c/s and 17 c/s. The proton at 4·10τ is coupled to two protons by 17 c/s and 1 c/s; and the proton at 4·60τ is coupled to two protons by 11 c/s and 1 c/s. These data based on coupling constants show that X is II.

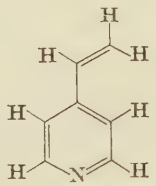
II



H_A at 3·38τ
H_B at 4·60τ
H_C at 4·10τ

The complete structure of the compound C_7H_7N is therefore, III.

III



EXAMPLE 5

This last example of the use of n.m.r. as a structural tool is intended to illustrate the full use of this technique in the elucidation of the structure of complex molecules in conjunction with i.r. and u.v. spectroscopy. It is taken from an actual study reported recently on the "Constituents of Thai Medicinal Plants—I. Aglaiol." (See D. Schiengthong, A. Verasam, P. Nanonggai-Suwanrath and E. W. Warnhoff, *Tetrahedron* **21**, 917 (1965).)

The analysis of aglaiol, m.p. 113–114°, $[\alpha]_D + 53°$, fitted best the molecular formula $C_{30}H_{50}O_2$. In the u.v. spectral region aglaiol exhibits only the rising end absorption of a single disubstituted double bond, ϵ_{210} 1175. The i.r. spectrum confirms the presence of a double bond (ν_{max} 3050 and 1640 cm^{-1}) probably present as a terminal methylene group (887 cm^{-1} ν_{max}), and reveals hydroxyl absorption (ν_{max} 3600 and 3450 cm^{-1}). The n.m.r. spectrum (Fig. 30) contains a broad peak at 5·24τ (2H) due to two vinyl hydrogen atoms; and an even broader multiplet at 6·77τ (1H) caused by a proton on a carbon atom bearing oxygen. Further upfield is a symmetrical triplet ($J = 6$ c/s) at 7·25τ (1H) assigned as a second proton on a carbon-bearing oxygen. The methyl region has five

peaks at 9·23, 9·15–9·13, 9·02, 8·73 and 8·70τ which were shown by integration to arise from seven methyl groups.

Consideration of this information strongly implicates a triterpene (30 carbons atoms including 7 methyl groups) with a side chain to permit the presence of the methylene group. The usual 3β-hydroxyl group is probably present since the 6·77τ peak (1H) is on the same position as the 3α-hydrogen of other 3β-hydroxytriterpenoids. The unusually low

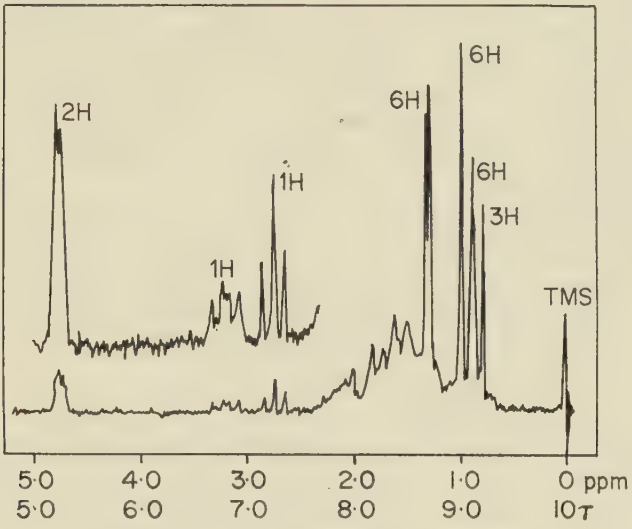
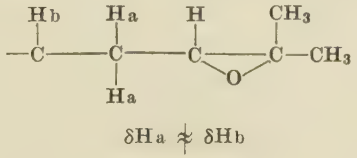


FIG. 30. The n.m.r. spectrum of Aglaiol.

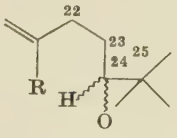
field position (8·73 and 8·30τ) of two of the methyl groups can be accounted for by the presence of the second oxygen atom on the carbon to which they are bound.

The second oxygen atom must then be a cyclic ether to account also for the 7·25τ triplet (1H). The symmetry of the triplet suggests that the single hydrogen on the carbon bearing oxygen is coupled only to one adjacent methylene group which is free to rotate about the connecting C—C bond, and furthermore, that any protons attached to the next carbon atom are appreciably chemically shifted from the methylene protons as in A. These conditions are readily satisfied by a modified



$\delta Ha \approx \delta Hb$

A



B

isoöctenyl side-chain B, in which the allylic C-22 hydrogen are chemically shifted from the C-23 methylene protons. To account for the apparent absence of any other double bonds in the molecule, aglaiol should thus be a dammarane derivative, more specifically (I) provided, of course, that it does belong to a known group of triterpenes.

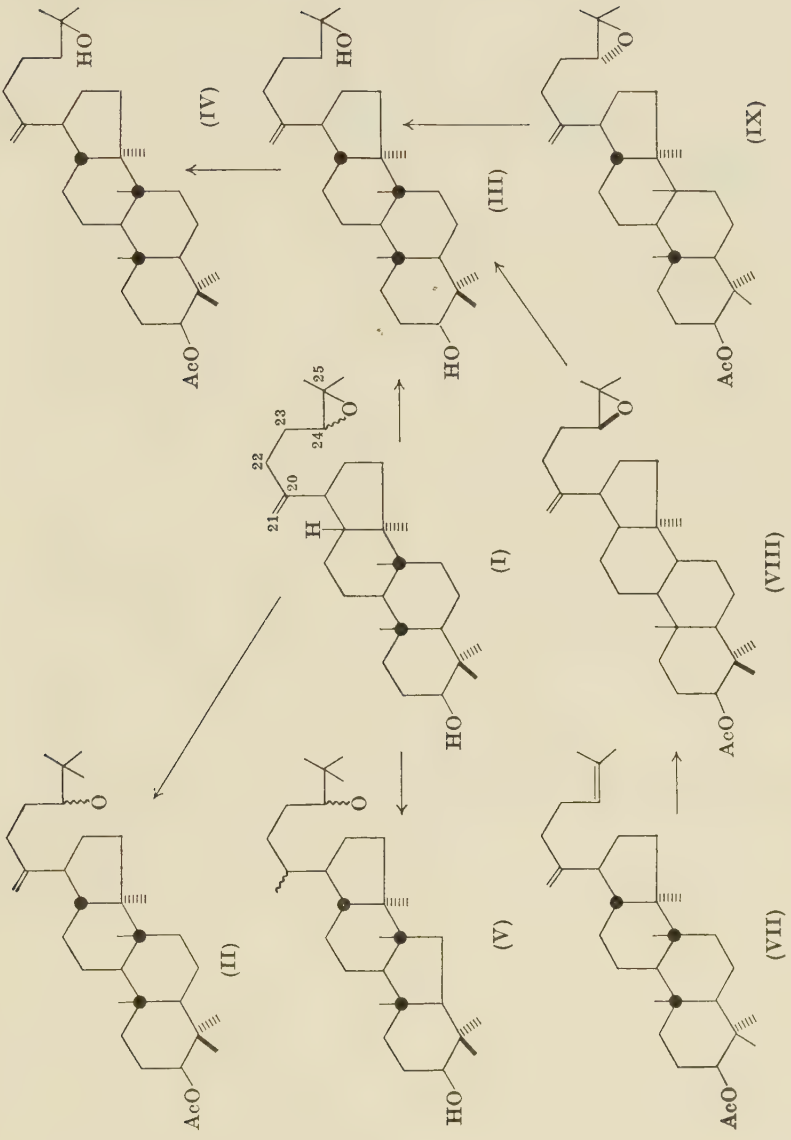
Support for this formulation is provided by the three high-field methyl n.m.r. resonance positions which correspond with those reported for the five fused quaternary methyl groups of analogous dammarane derivatives. (Ref.: J.-M. Lehn, *Bull. Soc. Chim. Fr.* 1832 (1962).)

Acetylation of aglaiol at room temperature gave a monoacetate (II) as the only product. Its i.r. spectrum contains an acetate carbonyl peak but no hydroxyl absorption. In the n.m.r. spectrum the acetate methyl group appears at 7·98τ and the 3α-hydrogen has undergone the characteristic shift to $\sim$5·60τ.

Hydrogenation of aglaiol in ethanol over palladium gave a dihydrocompound (V) which no longer contains a double bond; its i.r. spectrum lacks the peaks at 3050, 1640 and 887 cm^{-1}. The two vinyl hydrogen atoms have disappeared from the n.m.r. spectrum and an eighth methyl group is found to be present by integration. The peak at $\sim$7·32τ (1H) is still present but no longer a symmetrical triplet.

Aglaiol was reduced with LAH to a dihydro compound whose i.r. spectrum had increased hydroxy absorption as well as the peaks at 3060, 1640 and 887 cm^{-1} due to the doubly bonded methylene group. The n.m.r. spectrum of LAH-dihydroaglaiol still contains the broad peak (2H) from the vinyl hydrogens at 5·28τ and the broad multiplet at 6·80τ due to the 3α-proton, but the triplet centred at 7·26τ (1H) is missing as would be the case if an epoxide had been reductively cleaved at C-24 to yield (III). Acetylation of LAH-dihydroaglaiol at room temperature with acetic anhydride and pyridine produced a monoacetate whose i.r. spectrum has hydroxyl as well as acetate carbonyl absorption. Since the conditions used are those for acetylation of primary and secondary alcohols, the monoacetate is assigned the structure (IV) which was confirmed by shift of the 3α-proton from 6·80τ in (III) to 5·52τ in the n.m.r. spectrum of the monoacetate.

With chemical and physical evidence for the functional groups and presumptive evidence for the skeleton of (I), it was decided to substantiate this structure by a partial synthesis from a known dammarane derivative. Dammaradienyl acetate (VII) was epoxidized with one equivalent of monoperphthalic acid. Although the major product was the epoxide of the trisubstituted double bond (VIII) and (IX), each having the same R_f. on T.l.c. and, although it crystallized readily in beautiful needles, a pure compound could not be obtained. Therefore,


(I)
(II)
(III)
(IV)
(V)
(VII)
(VIII)
(IX)
HO
AcO
H
O
21
20
22
23
24
25

the entire peracid product was reduced with LAH to eliminate isomerism at C-24. From the reduction product was separated 35% of a component which, after recrystallization, was identical in all respects (m.p., mixed m.p., $[\alpha]_D$, i.r., n.m.r., t.l.c.) with LAH-dihydroaglaiol.

These examples are taken directly from the literature to illustrate how n.m.r. is used to solve structural problems that would have involved a considerable amount of chemical degradational work to have arrived at a structure.

General References

1. Jackman, L. M., "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon, New York, 1959.
2. Roberts, J. D., "Nuclear Magnetic Resonance Applications to Organic Chemistry", McGraw-Hill, New York, 1959.
3. Pople, J. A., Schneider, W. G., and Bernstein, H. J., "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, 1959.
4. Conroy, H., Nuclear Magnetic Resonance in Organic Structural Elucidation, *in* "Advances in Organic Chemistry", (R. A. Raphael, H. C. Taylor and Hans Wynberg, eds.), Vol. II, Interscience, New York, 1960.
5. Gutowsky, H. S., Nuclear Magnetic Resonance, *in* "Technique of Organic Chemistry", Vol. I, Part IV, 3rd ed., Interscience, New York, 1960.
6. Stothers, J. B., Applications of Nuclear Magnetic Resonance Spectroscopy, *in* "Technique of Organic Chemistry", Vol. XI, Part I, Interscience, New York, 1960.
7. Roberts, J. D., "An Introduction to the Analysis of Spin–Spin Splitting in High Resolution N.M.R. Spectra", W. A. Benjamin, New York, 1961.
8. Varian Associates, "High Resolution N.M.R. Spectra Catalogue", 1962.
9. Baldeschwieler, J. D. and Randall, E. W. Double Resonance Techniques, *Chemical Reviews*, **63**, 81, 1963.
10. Hall, G. G., Hardisson, A., and Jackman, L. M. Quantum Mechanical Interpretation of the Chemical Shift in Aromatic Molecules, *Tetrahedron*, **19**, Suppl. 2, 101, 1963.
11. A useful book for comparing experimental and theoretical spectra is "Interpretation of N.M.R. Spectra", Wiberg & Nist, Benjamin Inc., 1962.
12. Jardetzky, O., "Advances in Chemical Physics", Vol. 7, 499 pp., 1964. Wiley & Sons, London.
13. van Geet, L. A., and Hume, D. N. *Analytical Chemistry*, **37**, 979, 1965.

II. CHARTS AND CORRELATION TABLES

Charts and Correlation Tables

In the following pages we have collected a number of useful correlations, mainly for protons, but also for ^{19}F, ^{13}C and ^{31}P nuclei of chemical shift and spin coupling data. We also include a simple correlation chart for easy reference to show the approximate range for various functional groups.

The values for protons in various chemical environments are values (p.p.m.). The accuracy of the tables is within 0·1 p.p.m. for specific molecules, but for generalized cases the error may be as much as 0·5 p.p.m. This large difference may be the sum of a number of factors, such as the diamagnetic and paramagnetic contributions to the magnetic environment of the proton in question; the solvent being different from that used in establishing these correlations ($CDCl_3$); the reproducibility of the internal standard; and the performance of the n.m.r. spectrometer.

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CORRELATION CHART I. Protons (^1H Nuclei)

τ Value and Range *

TMS (reference material)

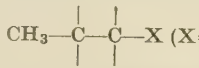
—CH_2—, cyclopropane

CH_4

ROH, monomer, very dilute solution

CH_3—C (saturated)

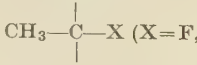
R_2NH, 0·1–0·9 mole fraction in an inert solvent

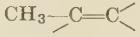


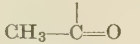
—CH_2— (saturated)

RSH

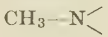
RNH_2, 0·1–0·9 mole fraction in an inert solvent







CH_3Ar



H—C≡C—, non-conjugated

H—C≡C—, conjugated

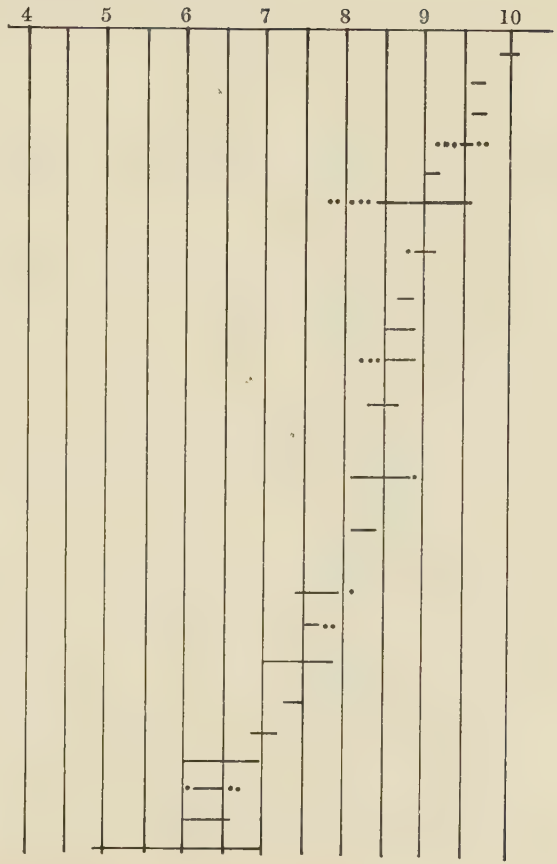
ArSH

CH_3—O—

$ArNH_2$, ArNHR and Ar_2NH

ROH, 0·1–0·9 mole fraction in an inert solvent

* Full line most probable range



Correlation Chart I—continued

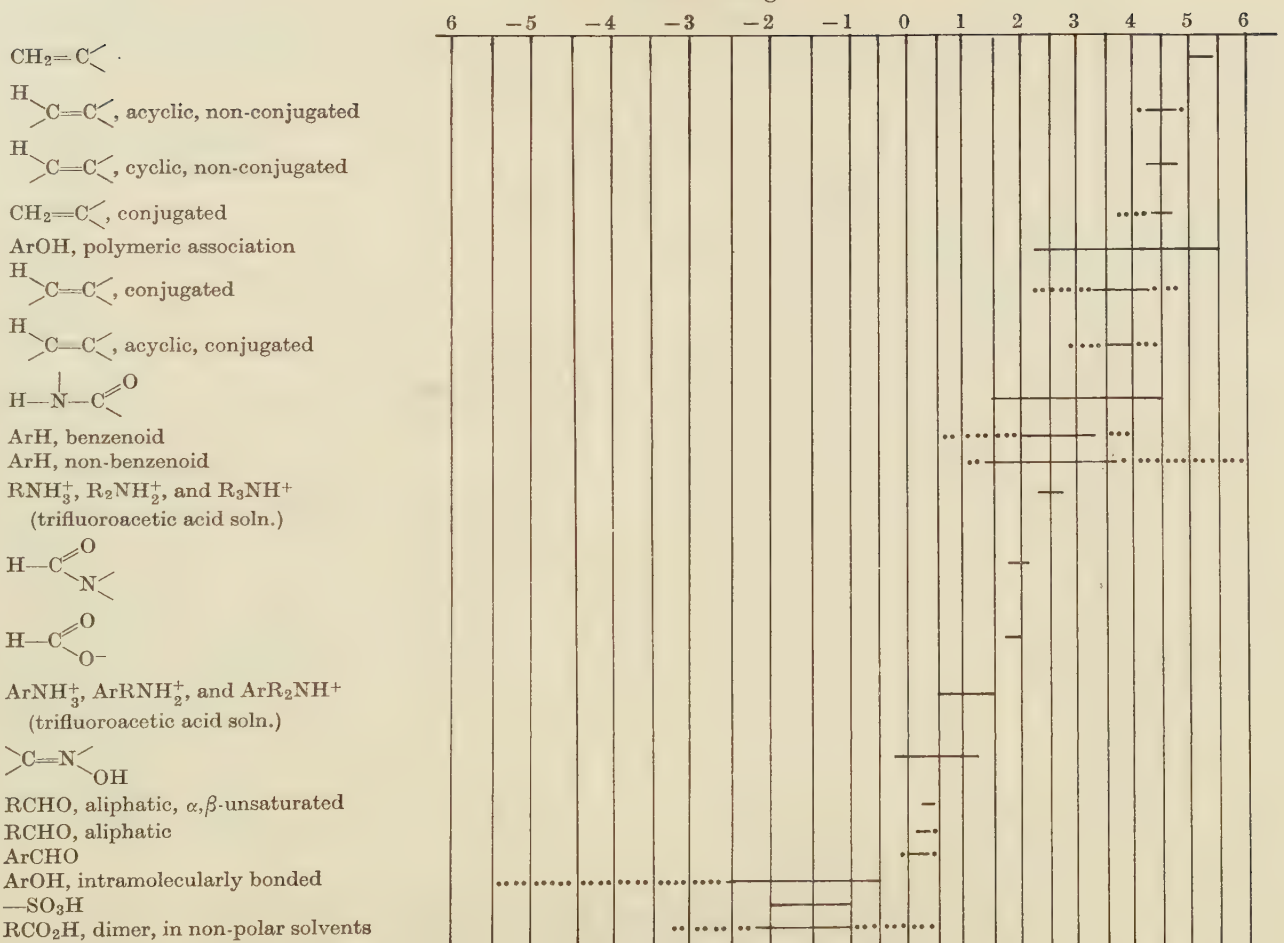


TABLE 4. τ Values of the Protons of CH_3, CH_2 and CH Group in Acyclic Molecules (R is an Alkyl Group)

X	CH_3X	$R'CH_2X$	$R'R''CHX$	X	CH_3X	$R'CH_2X$	$R'R''CHX$
—Mg I	11·3	10·62	10·20	—SO—	7·5		
—Li		10·99		—SCN	7·39	7·02	6·52
$—CH_3$	9·12	8·75	8·50	—COPh	7·38		6·42
RCH=CHCO—	8·14			—Br	7·30	6·70	5.97
—COOEt	8·05			—NMeCHO	7·22,		
—COOR	8·00	7·80			7·08		
$—CONH_2$	8·00	7·80		$—N(CH_3)Ph$	7·09		
—CN	8·00	7·52	7·3	—COBr	7·15		
$—COOCH_3$	7·95			—NHCOR	7·16	6·7	6·15
—CONHR				—Cl	7·00	6·56	5·98
$—SCH_3$	7·94						
—SH	7·92	7·60	6·90	$—\overset{\oplus}{N}R_3$	6·67	6·60	6·50
—COOH	7·90	7·64	7·42	—NCS	6·63	6·36	6·05
—COR	7·9	7·6	7·42	—OMe	6·73	6·64	6·44
$—NH_2$	7·85	7·50	7·13	—OH	6·62	6·42	6·12
$—N(Me)_2$	7·84	7·58		—OR	6·70	6·60	6·47
—CHO	7·83	7·80	7·62	$—SO_3H$	6·38		
$—NMeCH_2Ph$	7·83			—OCOR	6·29	5·80	4·9
—I	7·83	6·88	5·76	—OPh	6·27	6·10	6·0
$—NR_2$	7·81	7·50	7·12	—OCOPh	6·00	5·68	4·8
$—NMeCH_2CH_2OH$	7·73			$—OCOCF_3$	5·90	5·56	
—Ph	7·66	7·38	7·13	—F	5·70	5·66	5·4
—COSH	7·68			$—NO_2$	5·67	5·60	5·5
—SR	7·65	7·4					

Table 5

ALIPHATIC β-SUBSTITUENTS

The values given are shifts in p.p.m. from the values for hydrocarbons

$\tau CH_3 = 9{\cdot}10$—shift (p.p.m.)
$\tau CH_2 = 8{\cdot}75$—shift (p.p.m.)
$\tau CH = 8{\cdot}5$—shift (p.p.m.)

X	$CH_3—C—X$	$CH_2—C—X$	$CH—C—X$	$CH_3—C—C—X$
—F		0·17		
—Cl	0·62	0·58–0·32	0·02	0·14
—Br	0·81	0·63–0·30	0·24	0·14
—I	1·00	0·56–0·33	0·43	0·14
—OH, —OR	0·275	0·10		
—OCOR	0·37			
	0·40			
$—NH_2$, —NHR, $—NR_2$	0·10	0·05		
—SH, —SR	0·45	0·31		0·10
$—NO_2$	0·67			
—C=C	0·10	0·05		
—C≡C		0·05		
—CHO, —COR	0·18			
$—CO_2H$, $—CO_2R$	0·25			
—C≡N		0·42		
—Ph	0·35	0·35		

τ values of the protons of the ethyl group in some aliphatic esters

Compound	CH_2	CH_3
Diethyl fumarate	5·79	8·69
Diethyl maleate	5·81	8·69
Diethyl diethylmalonate	5·85	8·75
$Br(CH_2)_{10}COOCH_2CH_3$	5·92	8·75
Diethyl acetate	5·95	8·79
Diethyl orthoformate	6·50	8·81
Diethyl trifluoroacetate	5·61	8·59

The Additivity of Substituents

SHOOLERY'S RULES

The method is best used for the system Y—CH_2—X as it becomes rather unreliable for the system Y—CH$\begin{smallmatrix} X \\ \diagup \\ \diagdown \\ Z \end{smallmatrix}$. These constants apply only to acyclic systems and methylene groups.

$$\tau\text{-alkyl} = 9{\cdot}767 - \sum_i \sigma_i \text{ eff}$$

B. P. Dailey and J. N. Shoolery, *J.A.C.S.* **77**, 3877 (1955).

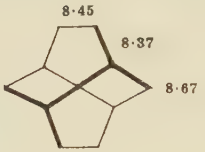
TABLE 6

Group	σ_i eff	Group	σ_i eff
—Br	2·33	—C=C	1·32
—Cl	2·53	—C≡C	1·44
—I	1·82	—Ph	1·85
—NR_2	1·57	—CF_3	1·14
—OH	2·56	—C≡N	1·70
—OR	2·36	—RCO	1·70
—OPh	3·23	—C(=O)OR	1·55
—OCOR	3·13		
—SR	1·64	—C(=O)NR_2	1·59
OH	0·47		

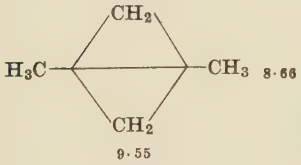
TABLE 7. Nuclear Magnetic Resonance of Some Cyclic Hydrocarbons and Functional Derivatives

Compound	τ CH_2	Compound	τ CH_2CO
Cyclopropane	9·78		
Cyclobutane	8·04	Cyclobutanone	6·97
Cyclopentane	8·49	Cyclopentanone	7·94
Cyclohexane	8·56	Cyclohexanone	7·78
Cycloheptane	8·46	Cycloheptanone	7·62
Cyclooctane	8·46	Cyclooctanone	7·70

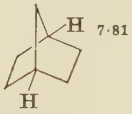
Adamantane. All protons 8·218

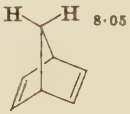


Twistane

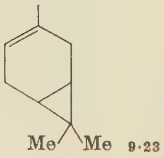


Δ^3-Carene





β-Pinene



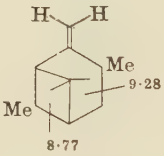


TABLE 8. α-Bromocyclohexanones and Other Cyclic Compounds

4-Phenylcyclohexanone	Configuration of —CHBr	τ value
cis-2-bromo	Axial	5·13
trans-2-bromo	Equatorial	5·62
cis,cis-2,6-dibromo	Axial	5·10
cis,trans-2,6-dibromo	Equatorial	5·38
4-t-Butylcyclohexanone		
cis-2-bromo	Axial	5·33
trans-2-bromo	Equatorial	5·71
cis,cis-2,6-dibromo	Axial	5·22
cis,trans-2,6-dibromo	Equatorial	5·42

TABLE 8 (continued)

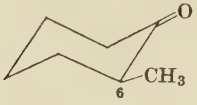
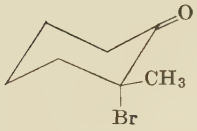
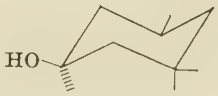
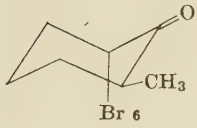
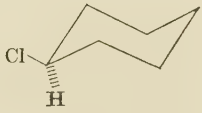
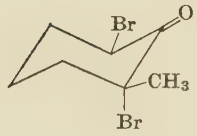
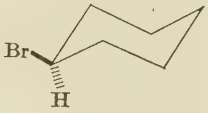
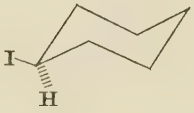
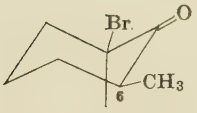
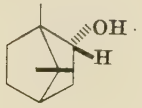
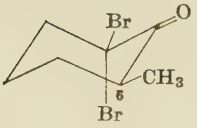
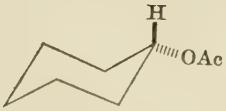
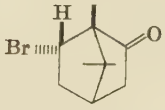
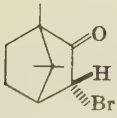
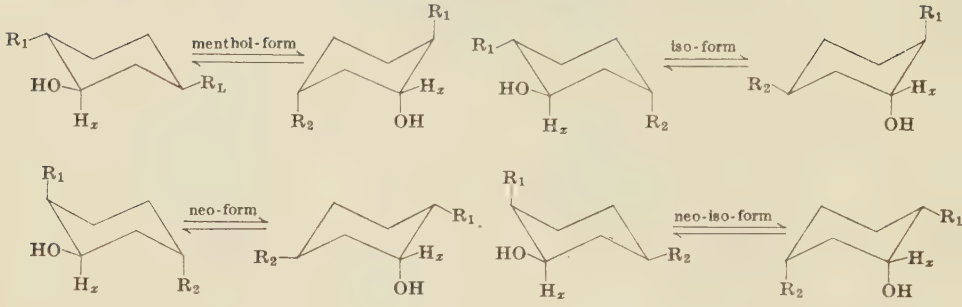
Compound	Alkyl	τ H-6	Compound	τ CH—X
	9·02	6·5		6·30
	8·20			5·95
	8·99	6·8		6·11
	8·06			5·89
				5·70
	8·92	6·5		6·31
	8·86	6·8		4·78
				5·82
				5·3

TABLE 9. Conformations of Various Menthols



		τ H_x	*J*ae	*J*ea	*J*ae	*J*ee	Equilibrium % of e conformer
Menthol form	Methyl menthol	6·92					100
	Menthol	6·62	9·4	4·2			
	Carvomenthol	7·02					100
	t-Butylmenthol	6·50	9·4	4·2			100
Iso-form	Iso-methylmenthol	6·27					74
	Iso-menthol	6·25	6·7	5·1			85
	Iso-carvomenthol	6·50					70
	Iso-t-butylmenthol	6·20	7·6	5·2			100
Neo-form	Neo-methylmenthol	6·53	Not split				
	Neo-menthol	5·95	Not split				
	Neo-carvomenthol	6·17			3·0	2·0	
	Neo-t-butylmenthol	5·85	Not split				
Neo-iso-form	Neo-iso-methylmenthol	6·30	10·5	4·5			100
	Neo-iso-menthol	6·05	Second order				29
	Neo-iso-carvomenthol	6·35	10·0	4·6			100
	Neo-iso-t-butylmenthol	5·77			3·6	2·2	

The axial proton absorbs at higher frequencies than its equatorial counterpart. This relationship is reversed for the 2,6-positions of cyclohexanones.

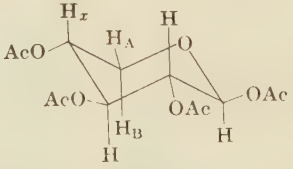


TABLE 10

Compound	δae (relative chemical shifts)
α- and β-D-Glucose pentaacetates	0·45
α- and β-D-Galactose pentaacetates	0·63
α- and β-D-Mannose pentaacetates	0·29
α- and β-D-Xylose tetraacetates	0·64
α- and β-D-Ribose tetraacetates	0·10
α-L and β-D-Arabinose tetraacetates	0·69

TABLE 11. τ Values of Protons in Cyclic Compounds Containing Heteroatoms

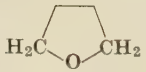
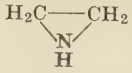
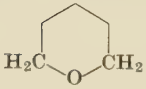
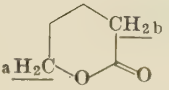
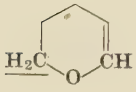
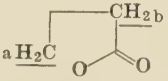
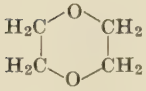
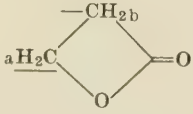
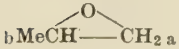
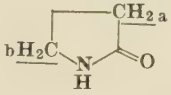
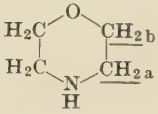
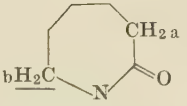
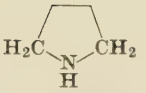
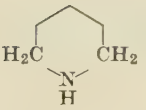
Compound	τ value	Compound	τ value
	6·37		8·17
	6·44		5·94a, 7·73b
	6·10		5·73a, 7·69b
	6·43		5·78a, 6·52b
	7·71a, 7·34b		7·77a, 6·63b
	7·17a, 6·43b		7·69a, 6·88b
	7·26		7·05
	7·31		

Table 12

ALDEHYDIC PROTONS

Compound	τ value	2,4-D.N.P.	τ value
Acetaldehyde	0·28	Acetaldehyde	2·42
Isobutraldehyde	0·43	Propionaldehyde	2·41
Crotonaldehyde	0·57	n-Butyraldehyde	2·43
Cinnamyldehyde	0·37	Isobutraldehyde	2·40
Benzaldehyde	0·03	α-Ethylbutyraldehyde	2·50
p-Chlorobenzaldehyde	0·07		
p-Methoxybenzaldehyde	0·20		
p-Dimethylaminobenzaldehyde	0·35		

ALCOHOLIC PROTONS IN ERYTHRO- AND THREO-ISOMERS ($CDCl_3$)

Compound	τ Erythro	τ Threo
2-Phenyl-2-butanol	7·0	7·8
2-Phenyl-3-pentanol	7·65	8·2
3-Phenyl-2-pentanol	6·4	7·4
4-Phenyl-3-hexanol	6·8	7·75
2,5-Dimethyl-4-phenyl-3-hexanol	8·05	9·2
1,2-Diphenyl-1-propanol	8·35	7·85
1,2-Diphenyl-2-methyl-1-butanol	8·25	7·65

ALCOHOLS, AMINES, THIOLS, AMIDES AND ACIDS

R—OH (pure)	9·5 − 6·0τ. Lower for enols; H-bonded enols usually −1 to −6τ. Lines are usually broadened singlet, but addition of a trace of acid sharpens the line and shifts its position between ROH and H_2O by exchange.
ArOH	5·5τ, lowered by hydrogen bonding.
R—OH	Position depends on concentration, temperature and solvent.
R—SH	9 − 8τ, lower for enthiols (*ca.* 5) broad lines.
ArSH	*ca.* 6·5.
RCO_2H	0 to −3τ. In non-polar solvents the —OH signal position is concentration independent. The signal is shifted by a trace of pyridine.
$RNH_2RR'NH$	8 − 5τ. Addition of a trace of acid gives a single line (exchange), solvent dependent, and between RNH_2 and H_2O. Concentrated acid $RNH_3^{\oplus}$ inhibits exchange, and the signal disappears because of coupling to N ($I=1$), triplet ($J_{NH}=ca.$ 50 c/s).
$RR'NH_2^{\oplus}$	Sharp low field line.
$RCONH_2$	5 − 1·5τ. Broad and often undiscernible, sharpened by alkaline catalysis of proton exchange.
=NOH	0 to −2τ.
RCONHCOR′	1–2τ broad.

TABLE 13. Olefinic Protons

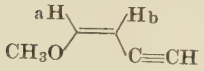
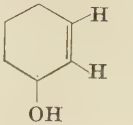
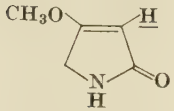
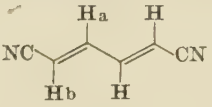
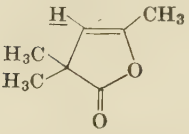
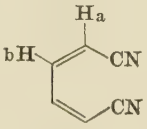
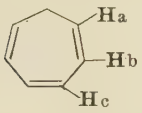
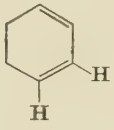
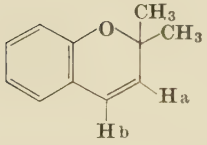
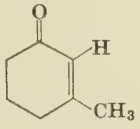
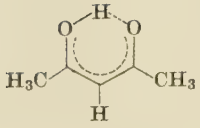
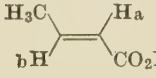
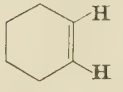
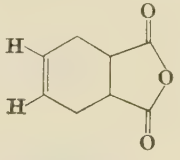
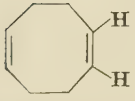
Compound	τ value	Compound	τ value
$CH_3(NH_2)C{=}\underline{CH}CO_2CH_3$	5·47	$(CH_3)_2C{=}\underline{CH}Cl$	4·32
	5·46a, 3·66b		4·28
$RHC{=}C{=}\underline{CH}_2$	4·99		
	4·95	$(CH_3)_2C{=}\underline{CH}CO_2H$	4·28
		$CH_2{=}\underline{CH}CH_2SCH_2\underline{CH}{=}CH_2$	4·28
$(CH_3)_2C{=}\underline{CH}.CH_2CH_2R$	4·88		4·26a, 2·96b
	4.84		
$(CH_3)_2C{=}\underline{CH}C{\equiv}CH$	4·83		4·25b, 2·66a
$(CH_3)_2C{=}\underline{CH}CH_3$	4·79		
	4·72a, 3·88b 3·45c	$(CH_3)_2C{=}\underline{CH}Br$	4·22
			4·22
	4·61a, 3·37b $J = 10·2$ c/s		
			4·18
	4·52		
			4·17a, 2·9b
		$(CH_3)_2C{=}\underline{CH}COR$	4·15
	4·43		4·14
	4·42		
$(CH_3)_2C{=}\underline{CH}CO_2CH_3$	4·38	$CH_2{=}\underline{CH}CH_2Ph$	4·12
$CH_3\underline{CH}{=}\underline{CH}CH_2OH$	4·32	$CH_2{=}\underline{CH}CH_2OCH_2\underline{CH}{=}CH_2$	4·12

TABLE 13 (continued)

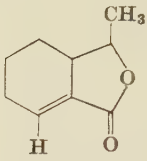
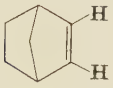
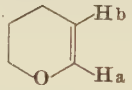
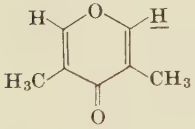
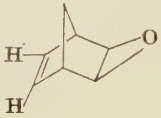
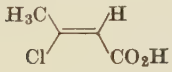
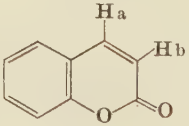
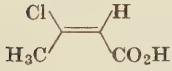
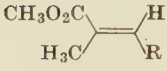
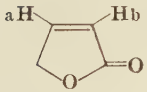
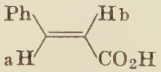
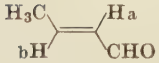
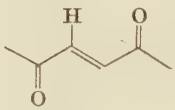
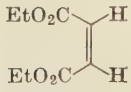
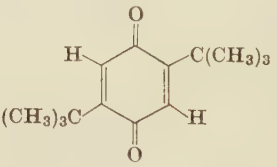
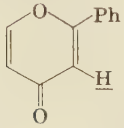
Compound	τ value	Compound	τ value
$CH_2{=}\underset{a}{CH}CH_2O\underset{b}{CH}{=}CH_2$	4·10a, 3·55b		3·73
$CH_2{=}CHCH_2NH_2$	4·08		
$CH_2{=}CHCH_2I$	4·07		
	4·06		3·63a, 5·45b
$(CH_3)_2C{=}CHCOCH_3$	4·03		
$CH_2{=}CHCH_2OH$	4·0		
	3·97		3·61
$CH_2{=}CHCH_2Br$	3·95	$CH_2{=}CHSCH_3$	3·58
	3·93		3·58a, 2·28b
	3·90		
	3·88		3·58
		$Cl_2C{=}CHCl$	3·55
	3·85b, 2·36a		3·54b 2·17a
	3·87a, 3·13b		3·53
	3·84		
$CH_2{=}CHCO_2CH_3$	3·80		3·53
	3·72		
		$CH_2{=}CHMgBr$	3·52 .J_{12}= 17·2 c/s

TABLE 13 (continued)

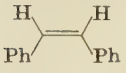
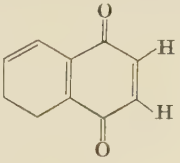
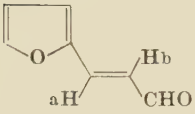
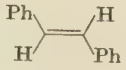
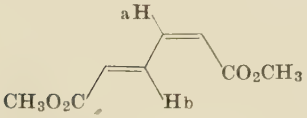
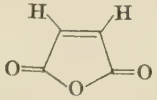
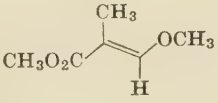
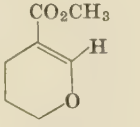
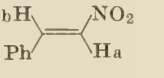
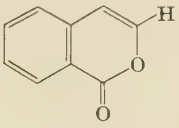
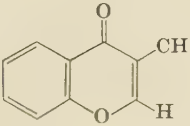
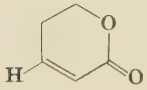
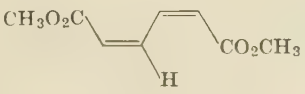
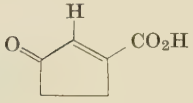
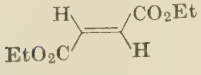
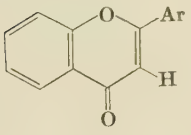
Compound	τ value	Compound	τ value
	3·51		3·03
	3·43b, 2·80a		2·99
	3·4a, 1·8b		2·90
PhCH=CHCHO	3·36	CH_2=CHOCOCH$_3$	2·75
	3·35		2·60
CH_2=CHSOCH$_3$	3·33		2·53
CH_2=CHPh	3·32		2·27a, 1·80b
CH_2=CHSiCl$_3$	3·25		2·23
PhCH=CHBr (b, a)	3·25a, 2·90b		2·22
	3·23		2·13
	3·23		
$(CH_3)_2$C=CHOCOCH$_3$	3·21		
$(Ph)_2$C=CHCH=C$(Ph)_2$	3·20		
	3·17		
	3·05		

TABLE 13 (continued)

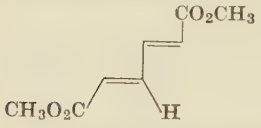
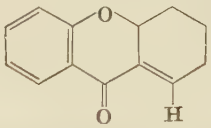
Compound	τ value	Compound	τ value
	2·66		2·42

TABLE 14. Olefinic Protons

METHYLENE GROUPS Coupling constants are given in a few cases.

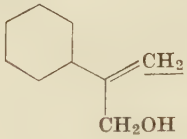
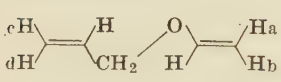
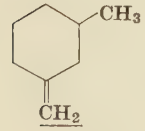
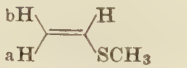
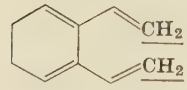
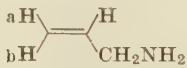
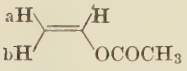
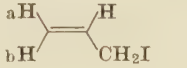
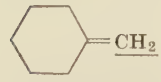
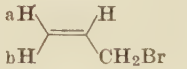
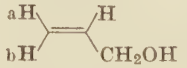
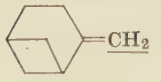
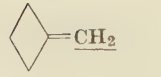
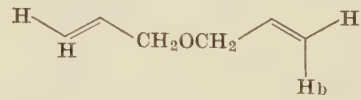
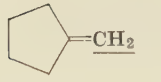
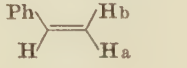
Compound	τ value	Compound	τ value
$RCH_2CH{=}CH_2$	5·90		5.10 $J = 0{\cdot}6$ c/s
	5·80a, 5·95b, 4·80c, 4·68d		
	5·50 $J = 1$ c/s		5·06a, 4·82b
		$CH_2{=}CH(CH_3)C{=}CH_2$	5·06
	5·6–3·4		4·97a, 4·87b
	5·45a, 5·15b		4·95a 4·85b
		$PhCH_2CH{=}CH_2$	4·97
	5·45		4·88a, 4·68b
$CH_2{=}C(CH_3)OCOCH_3$	5·38		
$(CH_3)_2C{=}CH_2$	5·34		4·87a, 4·75b
	5·33		
	5·30		4.83a, 4·75b
		$HC{\equiv}C.C(CH_3){=}CH_2$	4·74
	5·18		4·72a, 4·27b

TABLE 14 (continued)

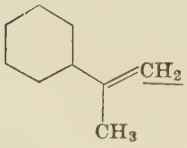
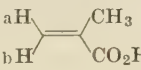
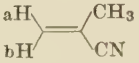
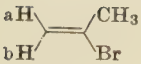
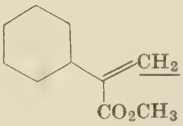
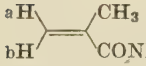
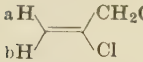
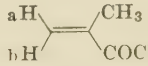
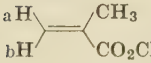
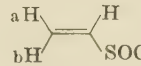
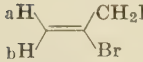
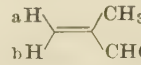
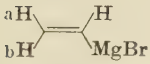
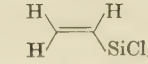
Compound	τ value	Compound	τ value
	4·66		J=7·4 c/s 4·29a, 3·70b
			4·28a, 4·18b
	4·67a, 4·48b		4·25, J=3·4 c/s
	4·62a, 4·23b		
$(Ph)_2C{=}\underline{CH_2}$	4·60		
	4·58a, 4·41b		4·08a, 3·88b
	4·51a, 3·97b		4·05a, 3·87b
	4·38a, 3·98b		3·93a, 3·63b
	4·34b, 4·02a		3·75

TABLE 15. τ Values of METHYL GROUPS α to a Double Bond

The methyl group referred to is underlined, and if two methyl groups are present in the same molecule, the respective τ values are indicated by the small letters a and b. *Cis/trans* geometrical isomerism is taken into account in this table, and where both methyl groups are underlined, their chemical shifts are the same irrespective of the geometry.

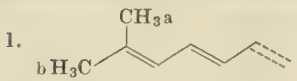
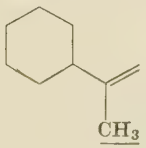
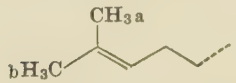
Compound	Methyl protons	Compound	Methyl protons
1. 	8·42a, 8·35b	5. $CH_2{=}C(\underline{CH_3})_2$	8·30
2. $(CH_3)_2C{=}CH\underline{CH_3}$	8·37	6. $\underline{CH_3}CH{=}CHCH_2OH$	8·30
3. $(CH_3)_2C{=}CHOAc$	8·35	7. 	8·27
4. 	8·34a, 8·28b		

TABLE 15 (continued)

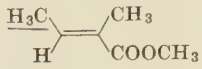
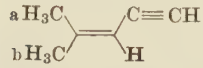
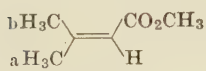
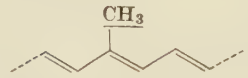
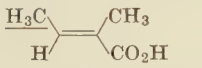
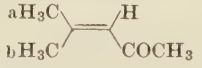
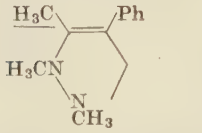
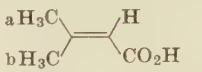
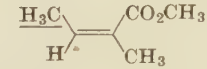
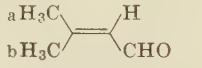
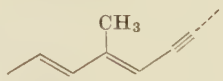
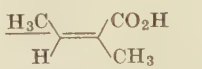
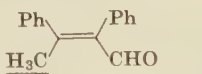
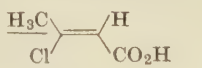
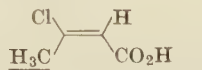
Compound	Methyl protons
8. 	8·25
9. $(\underline{CH_3})_2C{=}CHBr$	8·25
10. 	8·24a, 8·14b
11. $(\underline{CH_3})_2C{=}CHCl$	8·23
12. $CH_2{=}C(\underline{CH_3}).CH_2C(CH_3)_3$	8·23
13. $\underline{CH_3}.CH{=}CH.CH(OR)Ph$	8·20
14. $CH_2{=}C(\underline{CH_3}).CH{=}CH_2$ (*trans*)	8·16
15. 	8·16a, 7·88b
16. 	8·15–7·95
17. $CH_2{=}C(\underline{CH_3}).CH_2Cl$	8·13
18. 	8·13
19. $CH_2{=}C(\underline{CH_3}).COCH_3$	8·13
20. $CH(\underline{CH_3})$—$CH.CH$—$CHCO_2H$	8·13
21. 	8·14a, 7·94b
22. $CH_2{=}C(\underline{CH_3}).C{\equiv}CH$	8·11
23. $CH_2{=}C(\underline{CH_3}).OCOCH_3$	8·10
24. $CH_2{=}C(\underline{CH_3}).CO_2Et$	8·10
25. 	8·10
26. $\underline{CH_3}CH{=}CHCO_2H$	8·07
27. 	8·07a, 7·82b
28. 	8·05
29. 	8·04a, 7·89b
30. $CH_2{=}C(\underline{CH_3}).CONH_2$	8·04
31. $CH_2{=}C(\underline{CH_3}).CO_2H$	8·03
32. $CH_2{=}C(\underline{CH_3}).CN$	8·00
33. $\underline{CH_3}CH{\equiv}CHCHO$	7·97
34. $CH_2{=}C(\underline{CH_3}).COCl$	7·96
35. 	7·95–7·87
36. 	7·94
37. $CH_2{=}C(\underline{CH_3}).CONHPh$	7·94
38. CH_2 $C(\underline{CH_3}).CHO$	7·90
39. $CH_2{=}C(\underline{CH_3}).Ph$	7·86
40. 	7·85
41. $CH_2{=}C(\underline{CH_3})Br$	7·70
42. 	7·70
43. 	7·42

TABLE 16. Methylene Protons α to a Double Bond. τ Values (R is an Alkyl Group)

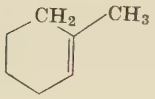
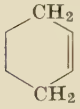
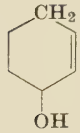
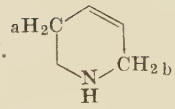
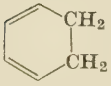
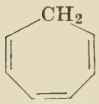
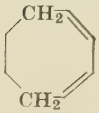
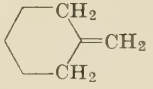
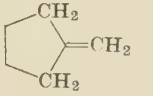
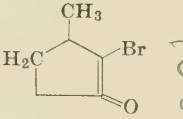
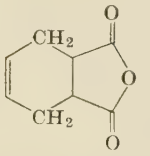
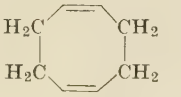
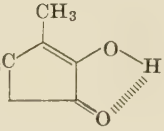
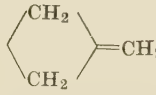
	Compound	Methylene protons
1.		8·14
2.	$(CH_3)_2{=}CHCH_2.CH_2CH_2CH_3$	8·11
3.		8·07
4.	$CH_2{=}CHCH_2R$	8·05
5.		8·04
6.		7·98
7.		7·93a, 6·67b
8.	$R{-}H_2C{-}CH{=}CH{-}CH_2{-}R$	7·90
9.	$CH_2{=}CHCH_2CH_2.CH{=}CH_2$	7·88
10.		7·84
11.		7·80
12.		7·80
13.		7·80
14.		7·78
15.		7·78
16.		7·64
17.		7·62
18.		7·57
19.		7·30
20.	$CH_2{=}CHCH_2CH{=}CH_2$	7·20
21.	$CH_2{=}CHCH_2SC(Ph)_3$	7·18
22.		7·10
23.	$CH_2{=}CHCH_2SCH_2CH{=}CH_2$	6·92
24.	$CH_2{=}CHCH_2CN$	6·85

TABLE 16 (continued)

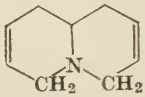
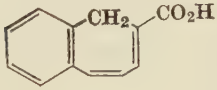
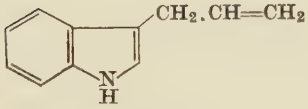
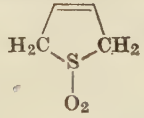
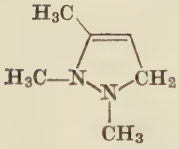
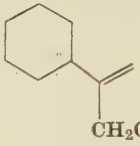
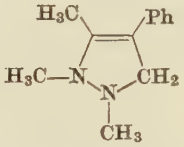
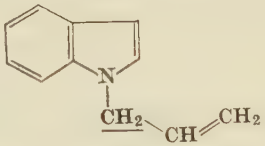
	Compound	Methylene protons
25.	$CH_2{=}CH.\underline{CH_2}Ph$	6·72
26.		6·70
27.	$CH_2{=}CH\underline{CH_2}NH_2$	6·70
28.		6·62
29.		6·55
30.	$CH_3CH{=}CH\underline{CH_2}SCN$	6·45
31.	$CH_2{=}CH\underline{CH_2}OH$	6·42
32.		6·26
33.		6·18
34.	$CH_2{=}CH\underline{CH_2}I$	6·13
35.	$CH_2{=}CH\underline{CH_2}Br$	6·07
36.	$CH_2{=}CH\underline{CH_2}O\underline{CH_2}CH{=}CH_2$	6·03
37.		5·97
38.		5·97
39.	$CH_3CH{=}CH\underline{CH_2}NCS$	5·96
40.	$Cl\underline{CH_2}CH{=}CH\underline{CH_2}Cl$	5·92
41.	$CH_3CH{=}CH\underline{CH_2}OH$	5·93
42.	$CH_2{=}C(Cl).\underline{CH_2}Cl$	5·85
43.	$CH_2{=}C(Br).\underline{CH_2}Br$	5·83
44.	$CH_2{=}CH.\underline{CH_2}NCS$	5·82
45.	$CH_2{=}CH\underline{CH_2}OCH{=}CH_2$	5·80
46.		5·50

TABLE 17. Methine Protons α to a Double Bond

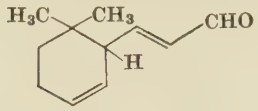
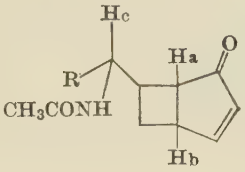
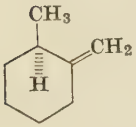
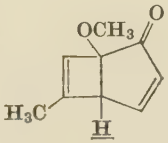
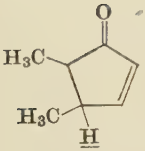
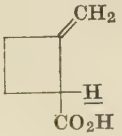
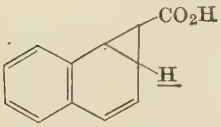
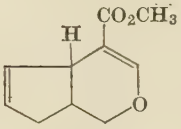
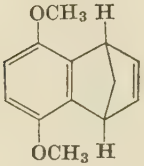
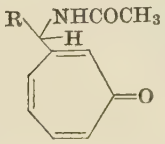
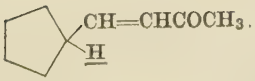
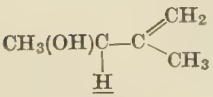
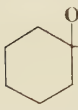
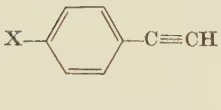
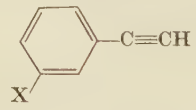
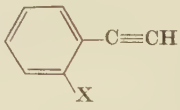
Compound		Compound	
	7·70		6·37a, 5·88b 5·16c
	7·60		6·31
	7·40		6·20
$(CH_3)_2\underline{CH}CH{=}CHCH_3$	7·37		
	7·28		5·98
	7·22		5·83
	6·42		5·38
	6·38		5·20

TABLE 18. Acetylenic Protons and Groups Attached to the Acetylenic Bond

Compound	τ value
$CH_3C{\equiv}\underline{CH}$* in $CDCl_3$	8·20
*$\underset{a}{\underline{HC}}{\equiv}C\underset{b}{\underline{CH_2}}OH$ in $CDCl_3$	7·67a, 5·72b
*$\underline{HC}{\equiv}\underline{CH}$ in $CDCl_3$	7·62
*$\underline{HC}{\equiv}CCH_2Cl$ in $CDCl_3$	7·60
*$\underset{a}{\underline{HC}}{\equiv}C.\underset{b}{\underline{CH}}(OH).CHCH_3$ in $CDCl_3$	7·53a, 5·28b
 in $CDCl_3$	7·52
$CH_2{=}C(CH_3)C{\equiv}\underline{CH}$ in $CDCl_3$	7·29
PhC≡CH in cyclohexane	7·26
PhC≡CH in $CDCl_3$	7·07
PhC≡CH pure compound	6·91
PhC≡CH in dioxane	6·50
$CH_3COC{\equiv}\underline{CH}$	6·83

* Indicates that signals are moved to lower field by a trace of pyridine and disappear on deuteration.

TABLE 19. Chemical Shifts of Acetylenic Protons in Substituted Phenylacetylenes

X	τ (Infinite dilution)	τ (Infinite dilution)	τ (Infinite dilution)
NH_2—	7·290		6·767
CH_3O	7·213	7·113	6·958
$(CH_3)_2CHO$—	7·213		
$(CH_3)_2CH$—	7·179		
$(CH_3)_3C$—	7·175		
CH_3—	7·172	7·138	6·885
F—	7·127		6·877
H—	7·125		6·807
Cl—	7·051		
Br—	7·042		
NO_2—	6·793	6·893	6·626
HO—			6·632

TABLE 20. The Effect of Substitution on the Proton Frequency of Benzene (2·73τ)

Substituent	Shifts relative to benzene (p.p.m.)		
	Ortho	*Meta*	*Para*
—NO_2	−0·97	−0·30	−0·42
—$COOCH_3$	−0·93	−0·20	−0·27
—COCl	−0·90	−0·23	−0·30
—CCl_3	−0·80	−0·17	−0·23
—CHO	−0·73	−0·23	−0·37
—$COCH_3$	−0·63	−0·27	−0·27
—COOH	−0·63	−0·10	−0·17
—CN	−0·30	−0·30	−0·30
—$CONH_2$	−0·50	−0·20	−0·20
—$NH_3^{\oplus}$	−0·40	−0·20	−0·20
—NHCOR	−0·40	−0·20	−0·30
—I	−0·30	−0·17	−0·10
—C≡C	−0·20	−0·20	−0·20
—OCOR	−0·20	+0·1	+0·2
—$CHCl_2$	−0·13	−0·13	−0·13
—SR	−0·1	+0·1	+0·2
—CH_2Cl	0·00	0·00	0·00
—Cl	0·00	0·00	0·00
—Br	0·00	0·00	0·00
—CH_2NH_2	+0·03	+0·03	+0·03
—CH_2CH_3	+0·07	+0·07	+0·07
—CH_2OH	+0·07	+0·07	+0·07
—CH_3	+0·15	+0·1	+0·1
—OCH_3	+0·23	+0·23	+0·23
—OH	+0·37	+0·37	+0·37
—$N(CH_3)_2$	+0·50	+0·20	+0·50
—NH_2	+0·77	+0·13	+0·40
—$NHCH_3$	+0·80	+0·30	+0·57

See example of Phenacetin

Table 21. Benzenoid Compounds

This short table lists a few useful correlations of aromatic protons in $CDCl_3$. The compounds are mainly *para* substituted.

Compound	Position	τ value	Attached groups
p-Bromo-fluorobenzene	3,5	2·62	
	2,6	3·10	
4-Chloronitrobenzene	3,5	2·48	
	2,6	1·83	
p-Chloroaniline	3,5	2·95	
	2,6	3·43	
p-Chlorobenzaldehyde	3,5	2·50	
	2,6	2·25	
p-Iodoanisole	3,5	2·47	—OCH_3, 6·25
	2,6	3·33	
p-Chloroacetophenone	3,5	2·55	—$COCH_3$, 7·42
	2,6	2·10	
p-Fluoroacetophenone	3,5	2·88	—$COCH_3$, 7·42
	2,6	2·03	
p-Trifluoromethyltoluene	3,5	2·52	—CH_3, 7·62
	2,6	2·75	
p-Anisaldehyde	3,5	2·98	—OCH_3, 6·13
	2,6	2·17	
p-Methoxybenzoic acid	3,5	3·02	—OCH_3, 6·12
	2,6	1·92	
p-Bromophenetole	3,5	2·72	—CH_2—, 6·07
	2,6	3·27	
p-Methylanisole	3,5	2·95	CH_3—, 7·72
	2,6	3·20	—OCH_3—, 6·25
p-Dimethylaminobenzaldehyde	3,5	3·31	
	2,6	2·29	
p-Cymene	2,3,5,6	2·92	—CH_3, 7·70
p-Xylene	2,3,5,6	2·95	CH_3—, 7·70
Acetone-2,4-dinitrophenyl hydrazone	3	0·95	
	5	1·77	
	6	2·10	
3,4-Dimethoxybenzaldehyde	2	2·60	
	5	3·02	
	6	2·55	
Mesitylene	2,4,6	3·22	7·25
m-Phenylenediamine	2	3·97	
	4,6	3·89	
	5	3·07	
2,5-Dimethoxyaniline	3	3·29	
	4	3·75	
	6	3·68	
2,4-Dinitroanisole	3	1·28	
	5	1·53	
	6	2·72	
3,5-Diphenyl-4-hydroxy benzaldehyde	2,6	2·17	
m-Terphenyl	2	2·23	
o-Terphenyl	2,3,4,5	2·60	
p-Terphenyl	2,3,5,6	2·34	

TABLE 22. Phenols

Ref.: R. J. Highet and P. F. Highet, *J. Org. Chem.* **30**, 902 (1965).

Phenols (in $CDCl_3$)				Acetates		
	o	*m*	*p*	*o*	*m*	*p*
p-Methoxyphenol	3·23	3·23		2·98	3·08	
2,6-Dimethoxyphenol		3·41	3·20		3·37	2·87
p-Cresol	3·26	2·97		3·02	2·83	
2,6-Dimethylphenol		3·02	3·24		2·97	2·97
3,5-Dimethylphenol	3·53		3·43	3·28		3·13
2,4-Dimethylphenol	3·33	3·05–3		3·10	2·97–3	
		3·12–5			3·00–5	
2,5-Dimethylphenol	3·47	3·00	3·33	3·15	2·88	3·05
2-Methoxy-4-methylphenol	3·17	3·32–3		3·07	3·17–3	
		3·34–5			3·32–5	
2-Methoxy-5-methylphenol	3·32	3·25	3·38	3·12	3·14	3·02
Methyl syringate		2·67			2·63	
Vanillin	2·93	2·55		2·76	2·47–3	
					2·49–5	
Isovanillin	2·56	3·04	2·57	2·41	2·93	2·23
p-Nitrophenol	3·07	1·80		2·83	1·87	
p-Chlorophenol	3·22	2·80		2·95	2·67	
p-Hydroxybenzaldehyde	3·00	2·15		2·71	2·07	
Phenols (in DMSO)						
p-Hydroxyacetophenone	3·10	2·13				
4-Hydroxy-2-methylacetophenone	3·28–2 3·27–6	2·20				
4-Hydroxy-3-methylacetophenone	3·10	2·23–2 2·30–6				
Vanillalacetone	3·15	2·65–3 2·82–5				
7-Hydroxy-4-methylcoumarin	3·14–6 3·25–8	2·39				
2,5-Dichlorophenol	2·97	2·62	3·13			
2-Hydroxy-4-methoxyacetophenone	3·50	2·14	3·47			

TABLE 23. Methoxybenzenes

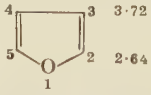
Ref.: A. Zweig, J. E. Lehnsen, J. E. Lancaster and M. T. Neglia, *J.A.C.S.* **85**, 3940 (1963).

Compound in CCl_4	Positions	τ value	CH_3O—
Methoxybenzene	2,6	3·26	
	3,5	2·80	6·26
	4	3·26	
1,2-Dimethoxybenzene	3,6	3·25	6·23
	4,5	3·25	
1,3-Dimethoxybenzene	2	3·72	
	4,6	3·61	6·28
	5	2·95	
1,4-Dimethoxybenzene	2,3,5,6	3·31	6·32
1,2,3-Trimethoxybenzene	4,6	3·56	1,3-, 6·22
	5	3·18	2-, 6·28
1,2,4-Trimethoxybenzene	3	3·65	1-, 6·32
	5	3·78	2-, 6·28
	6	3·36	4-, 6·24
1,3,5-Trimethoxybenzene	2,4,6	4·09	6·30
1,2,3,4-Tetramethoxybenzene	5,6	3·58	1,4-, 6·22; 2,3-, 6·26
1,2,3,5-Tetramethoxybenzene	4,6	4·05	1,3-, 6·23; 2-, 6·36; 5-, 6·32
1,2,4,5-Tetramethoxybenzene	3,6	3·57	6·27
Pentamethoxybenzene	6	3·83	1,5-, 6·23; 2,4-, 6·30; 3-, 6·18

Similar series are reported for the chloro and methylbenzenes. "High-resolution Nuclear Magnetic Resonance", J. A. Pople, W. G. Schneider and H. J. Bernstein, McGraw-Hill Book Company Ltd., 1959, pp. 259–263.

TABLE 24. Furanoid Compounds

Ref.: Furans and Thiophenes, J. B. Leane and R. E. Richards, *Trans. Faraday Soc.* **55** (436), Part 4 (1959).

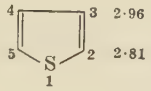


$J_{2,3}$ 1·8, $J_{3,4}$ 3·5, $J_{2,4}$ 0·8, $J_{2,5}$ 1·6 c/s

Solvent $CDCl_3$ unless otherwise stated.

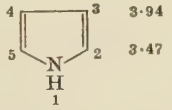
Substituents	Positions, τ values 2	3	4	5	Other attached groups
2-Me		4·12	3·85	2·82	Me, 7·62
2,5-Me_2		4·20	4·20		
2-OH		3·67	3·67	2·52	
2-CHO		2·72	3·37	2·28	—CHO, 0·33
2-CO_2H		2·43	3·20	2·52	
3-CO_2H	2·12		3·40	2·70	
4,5-Ph; 2-CHO		2·81			
2-CH_2SH		3·83	3·72	2·67	—CH_2—, 6·27
2-CH_2OH		3·67	3·67	2·56	—CH_2—, 5·43
2-CH_2NH_2		3·87	3·70	2·67	—CH_2—, 6·20
2-CH=CHCHO		3·23	3·45	2·45	
2-CH_2OCOCH_3		3·62	3·65	2·60	—CH_2—, 4·97
2-$COCH_3$, 5-Me		2·88	3·83		Me-, 7·62; —COMe, 7·57
2-COEt, 5-Me		2·92	3·87		Me-, 7·62; —$COCH_2$—, 7·22
2-CO_2Me		2·80	3·49	2·42	—CO_2CH_3, 6·12

TABLE 25. Thiophene and its Compounds



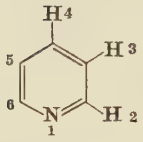
Substituent	Positions, τ value 2	3	4	5	Other attached groups
2-NO_2		2·31	2·89	2·41	
2-OCH_3		3·89	3·41	4·14	
2-$COCH_3$		2·36	2·90	2·36	
2-CHO		2·31	2·86	2·21	—CHO, 0·08
2-CO_2H		2·29	2·89	2·29	
2-SO_2CH_3		2·21	2·84	2·21	
3-$COCH_3$	1·66		2·26	2·46	
3-SO_2CH_3	1·74		2·56	2·44	
3-OCH_3	3·92		3·34	3·06	
3-SCH_3	3·09		3·09	2·86	
3-CO_2H	1·81		2·56	2·56	
3-CHO	1·84		2·31	2·31	
3-CH_3	3·31		2·31	2·06	
2-CH_3		3·28	3·13	2·97	—CH_3, 7·52
2-$COCH_2CH_3$		2·30	2·90	2·40	—CH_2—, 7·07; CH_3—, 8·77
2-$COCH_3$, 5-CH_3		2·50	3·22		—CH_3, 7·48; —$COCH_3$, 7·52
2-I		2·79	3·23	2·69	
2-SH, 5-Cl		3·12	3·28		

TABLE 26. Pyrrole and Its Compounds



Substituent	Positions 2	3	4	5	Other attached groups
2-CHO		2·83	3·70	3·02	—CHO, 0·55
2-Me, 3-n-Amyl			4·02	3·45	2-Me, 7·85; —CH_2—, 7·62
3-Propyl	3·45		3·87	3·30	—CH_2—, 7·52
1,5-Me_2, 2-CHO		3·19	3·98		1-Me, 6·13; 5-Me, 7·73
1-Me, 2-$COCH_3$		3·23	3·90	3·08	1-Me, 6·08
2-CH_2CH_3		4·03	3·83	3·32	—CH_2—, 7·37; CH_3—, 8·77
2,4-Me_2		4·27		3·63	7·80, 7·93

TABLE 27. Pyridine and Its Compounds



2-H, 1·5, 3-H 3·01, 4-H 2·64

$J_{2,3}$ 5·5, $J_{3,4}$ 7·5, $J_{2,4}$ 1·9, $J_{3,5}$ 1·6, $J_{2,6}$ 0·4, $J_{2,5}$ 0·9 c/s

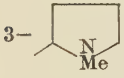
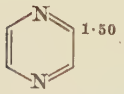
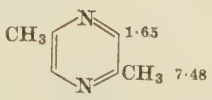
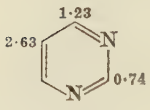
Substituent	Position 2	3	4	5	6	Other attached groups
2-CH=CH_2		2·73	2·45	2·92	1·48	
2-CH_2CONH_2		2·75	2·35	2·83	1·48	—CH_2—, 6·28
2,6-Me_2		3·05	2·55	3·05		—CH_3, 7·48, see later table
3- 	1·40		2·25	2·70	1·45	
4-$SCH_2CH_2CH_3$	1·62	2·90		2·90	1·62	
2-CH_2Ph			2·46		1·44	—CH_2—, 5·82
N-methyl-2-pyridone					2·69	N-Me, 6·49
3-OH	1·92				1·71	
2-NH_2				3·36	1·91	
3-$CONH_2$	0·96		1·84	2·62	1·25	
3-Me, N-oxide	1·90					Me, 7·67
(D_2O) 1-N-Ph, 3-$\overset{\oplus}{C}ONH_3$ $\overset{\ominus}{I}$	0·63		1·03	1·71	0·88	—CH_2, 5·26
5-Me, 2-CH_2OEt		2·68	2·68		1·73	—CH_3, 7·72

TABLE 28

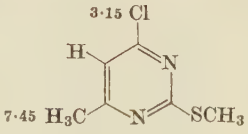


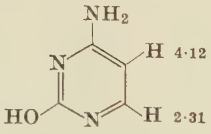
Pyrazine





Pyrimidine





Cytosine (D_2O)

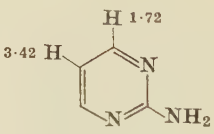
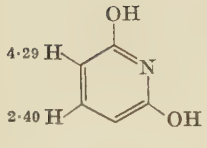
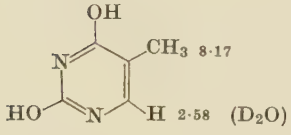


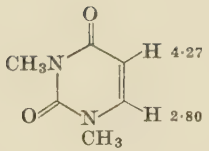
TABLE 28 (continued)

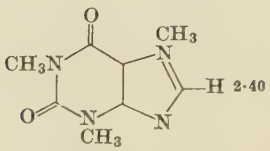


Uracil (D_2O)

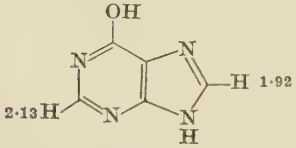


Thymine

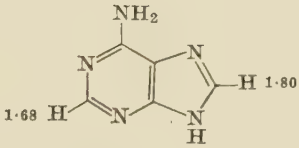




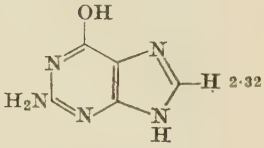
Caffeine



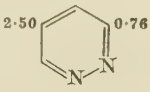
Hypoxanthine (D_2O)



Adenine (D_2O)

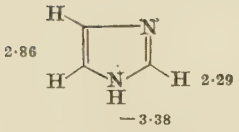


Guanine (D_2O)

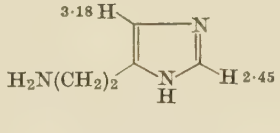


$J_{2,3}$ 3·7 c/s

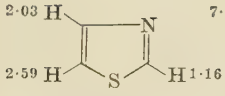
Pyridazine



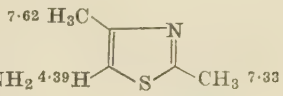
Imidazole

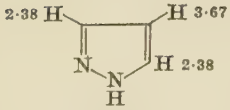


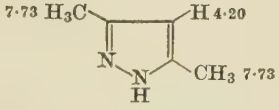
Histamine



Thiazole



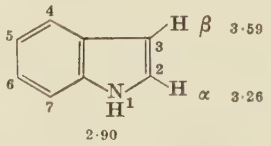




Pyrazole

TABLE 29. Indole and Derivatives (in $CDCl_3$ Unless Otherwise Indicated)

Ref.: R. V. Jardine and R. Brown, *Can. J. Chem.* **41**, 2067 (1963); L. A. Cohen, J. W. Daly, H. Kny and B. Witkop, *J.A.C.S.* **82**, 2184 (1960).

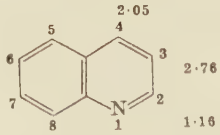


in $CDCl_3$

Substituent	α	β	—Me	—CH_2
3-Me	3·39		7·70	
2-Me		3·95	7·80	
2-CO_2Et		2·80 DMSO		
3-CO_2Et	1·88 DMSO			
3-$COCH_3$	1·66 DMSO			
3-CO_2H	1·82 DMSO			
2-CO_2H		2·80 DMSO		
3-COPh	2·0 DMSO			
2-COPh		2·54		
3-Br	2·96			
N-Me	3·18	3·52	6·63	
3-$CH_2CH_2NH_2$	3·08			7·05
2,3-Me_2			7·95, 7·88	
3-Ph	2·97			
N-Me-2-Ph		3·47	6·43	
2,5-Me_2		3·90	2-Me, 7·72	5-Me, 7·60
3-$CH_2CH(NH_2)CO_2H$	2·72 D_2O			CH_2, 6·90, 6·67; CH, 6·25
3-$COCONMe_2$	2·31			4-H 1·73
2-Me, 5-Cl		3·90	4-H, 2·56	6-H, 2·98; 7-H, 2·98

TABLE 30

QUINOLINE



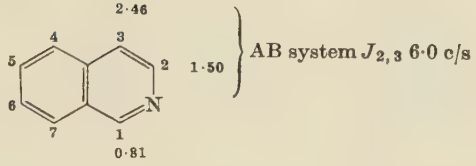
ABX group. $J_{3,4} = 7{\cdot}3$, $J_{2,3} = 5{\cdot}0$, $J_{7,8} \sim 7$ c/s

Substituent	2	3	4	8	5	7	CH_3
2,4-Me_2		2·86					2-Me, 7·30; 4-Me, 7·34
2,6-Me_2		2·79	2·10	2·10			2, 7·28; 6, 7·50
6-OCH_3	1·29	2·72	2·03	2·03	3·00	2·65	—OCH_2, 6·13
8-Me	1·28	2·88	2·18				7·23
5,7-Me_2	1·38	2·95	2·09	2·05			7·65, 7·57
5.7-Cl_2	1·18	2·66	1·61	2·43			

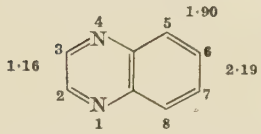
Coupling constants for 5,7-Me_2: $J_{2,3}$ 3·9, $J_{3,4}$ 8·6, $J_{2,4}$ 1·7, $J_{4,8}$ 0·8 c/s

TABLE 30 (continued)

ISOQUINOLINE



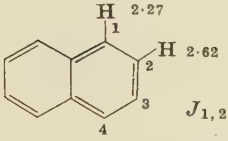
QUINOXALINE



2,3-Me_2, 5,8-OH_2	2·97 (6,7)	2,3-Me_2, 7·28

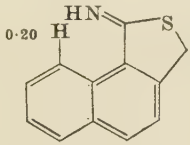
TABLE 31. Condensed Aromatic Hydrocarbons

NAPHTHALENE



Substituent	1	2	3	4	5	6
2,3-Br_2	1·95			1·95		
1,4-$(NO_2)_2$		1·93	1·93			
1,4-Naphthoquinone		3·03	3·03		1·93	2·23

An interesting example is the following Naphthalene derivative



ANTHRACENE

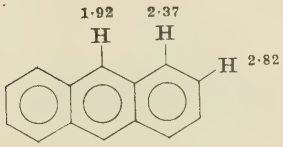
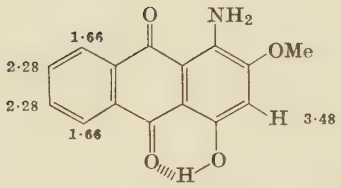
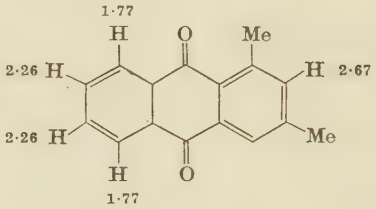
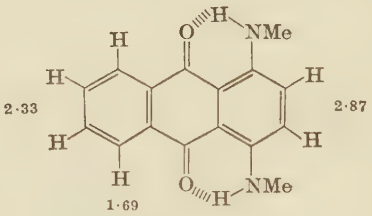


TABLE 31 (continued)

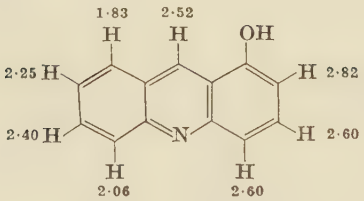
Substituent	1	2	CH_2
9,10-Br_2	1·43	2·40	
9,10-Cl_2	1·48	2·40	
Anthrone	1·64		
9,10-H_2	2·82	2·82	6·13

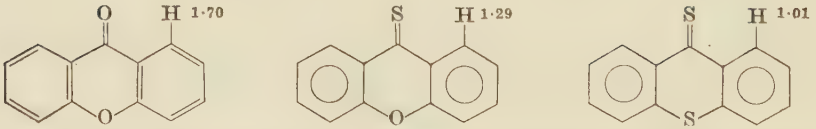




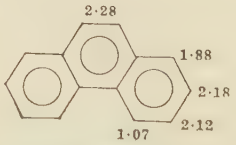


1-Hydroxyacridine





Ref.: Polycondensed systems. R. H. Martin, N. Defay and F. Geerts-Evrard, *Tetrahedron* **21**, 1833 (1965).

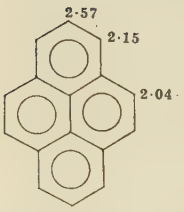


Phenanthrene

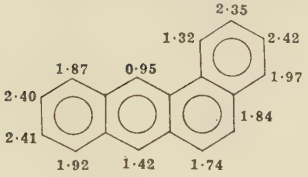
$J_{1,2}$ 8·4, $J_{1,3}$ 1·6, $J_{1,4}$ 0·5, $J_{2,3}$ 7·3, $J_{2,4}$ 1·6, $J_{3,4}$ 8·4. cps

Ref.: P. M. G. Bavin, K. D. Bartle and J. A. S. Smith, *Tetrahedron* **21**, 1087 (1965).

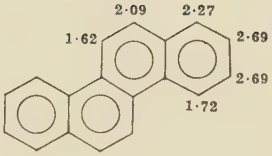
TABLE 31 (continued)



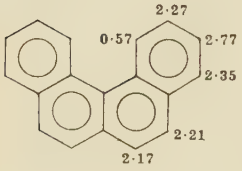
Pyrene



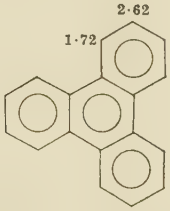
1,2-Benzanthracene



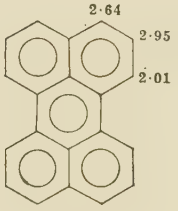
Chrysene



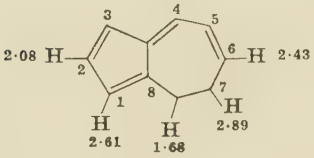
3,4-Benzphenanthrene



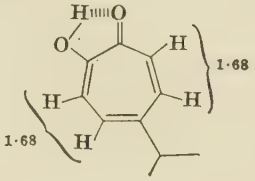
9,10-Benzphenanthrene



Perylene

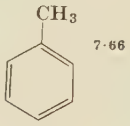


Azulene J_{12} 3·8, $J_{45} = J_{56} = 10·0$

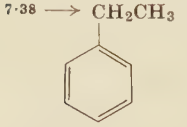


γ-Thujaplicin

TABLE 32. Toluene Methyl Group. (See Other Tables Also)

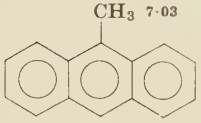


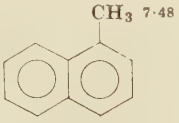
Substituent	*o*	*m*	*p*
—OH	7·71	7·73	7·70
CH_3COO—			7·68
Me—	7·71	7·73	7·70
$PhCH_2$—			7·73
F			7·70
$COCH_3$			7·60
—CO_2Me	7·15	7·73	7·48
NO_2	7·47	7·58	7·57

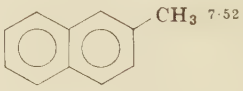


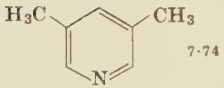
—CH_2OH	5·60
—CH_2Br	5·57
—CH_2OMe	5·6
—CH_2NH_2	6·44

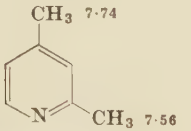
Miscellaneous Me Groups (See in Tables of Aromatic Protons)











N.B. CH_3, CH_2, CH attached to naphthyl and higher hydrocarbons, and to α-pyridyl, pyrimidyl, furyl, thienyl, thiazolyl, etc., appear at values 0·05 to 0·65 lower than in toluene.

CH_3, CH_2, CH attached to pyrryl, β- or γ-pyridyl come at values 0·05 to 0·3 higher than in toluene (see tables).

Table 33. N-Methyl Groups

Ref.: J. C. N. Ma and E. W. Warnhoff, *Can. J. Chem.* 1849 (1965).

This reference contains a correlation table of over 100 *N*-methyl groups. A few representative examples are given here to illustrate especially the large chemical shift observed when the solvent is changed from deuterochloroform to trifluoroacetic acid.

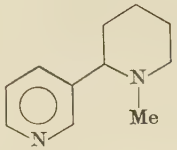
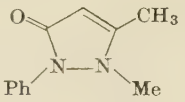
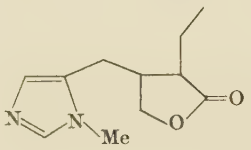
Compound	Structure	A τ $CDCl_3$	B τ CD_3COOD	C τ CF_3COOH	B–C	C–B	C–A
Methyldiethylamine	$(CH_3CH_2)_2NMe$	7·81	7·24	7·02	+0·57	+0·22	+0·79
N,*N*-Dimethylbenzylamine	$PhCH_2NMe_2$	7·78	7·14	6·98	+0·64	+0·16	+0·80
Nicotine		7·85	7·15	6·90	+0·70	+0·25	+0·95
	Sec Aliphatic amines						
N-Methyl-n-butylamine	$CH_3(CH_2)_3NHMe$	7·57	7·24	7·04	+0·33	+0·20	+0·53
N-Methylbenzylamine	$PhCH_2NHMe$	7·58	7·24	7·06	+0·34	+0·18	+0·52
Ephedrine	$PhCH(OH)—CH(NMe)CH_3$	7·66	7·12	6·99	+0·54	+0·13	+0·67
	Aromatic and *N*-heteroaromatic amines						
N-Methylaniline	$PhNHMe$	7·34	7·22	6·83	+0·12	+0·39	+0·51
N,*N*-Dimethylaniline	$PhNMe_2$	7·15	6·99	6·54	+0·16	+0·45	+0·61
Antipyrine		6·98	6·75	6·42	+0·23	+0·33	+0·56
Pilocarpine		6·43	6·10	6·04	+0·33	+0·06	+0·39

TABLE 33 (continued)

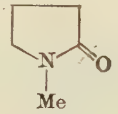
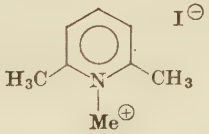
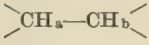
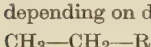
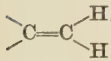
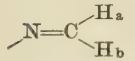
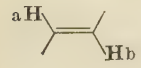
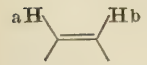
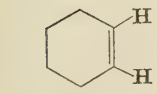
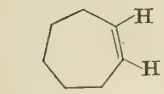
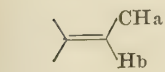
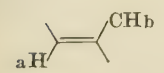
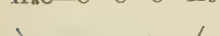
Compound	Structure	A τ $CDCl_3$	B τ CD_3COOD	C τ CF_3COOH	B–C	C–B	C–A
		Amides and imides					
N,*N*-Dimethylformamide		7·15	7·13	6·95	+0·02	+0·18	+0·20
N-Methyl-2-pyrrolidone		7·18	7·18	6·91	0·00	+0·27	+0·27
		Quaternary ammonium compounds					
Tetramethyl ammonium iodide		Insol.	6·70	6·65	—	+0·05	—
1,2,6-Trimethylpyridinium-iodide		Insol.	5·81	5·76	—	+0·05	—

TABLE 34. Proton–Proton Spin Coupling Constants

Group	J_{ab} c/s
	−10 to −18 depending on the electronegativities of the attached groups. Refs. 1, 2 and 3.
	0–12 depending on dihedral angle (4).
	6·7–7·2
	5·7–6·8
	−3 to +7
	8–16
	11–19
	5–14
	3–6
	1·6
	9–14
	4–10
	0 to −2
	0–2
	10–13

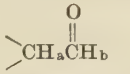
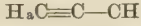
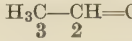
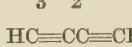
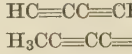
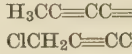
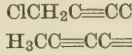
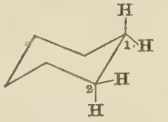
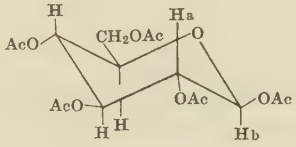
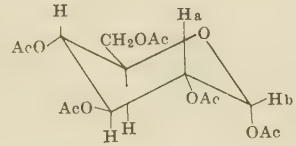
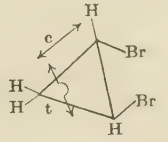
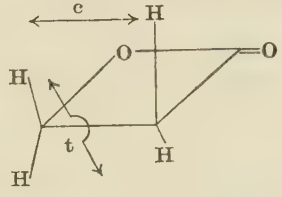
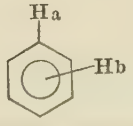
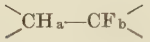
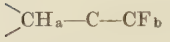
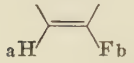
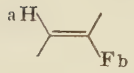
Group	J_{ab} c/s
	1–3
	2–3
	J_{12} 5·8, J_{13} 2·4, J_{23} 7·2
	2·2
	1·2
	1·0
	0·4
	$J_{11} \sim 12$, J_{12} 5–8 (aa) J_{12} 2–3·5 (ae) J_{12} 2–3·5 (ee)
	J_{ab} 8
	J_{ab} 3·2
	$J_c = J_t = 6·3$
	$J_c = J_t = 6·1$
	*o*, 7–10 *m*, 2–3 *p*, 1 or less

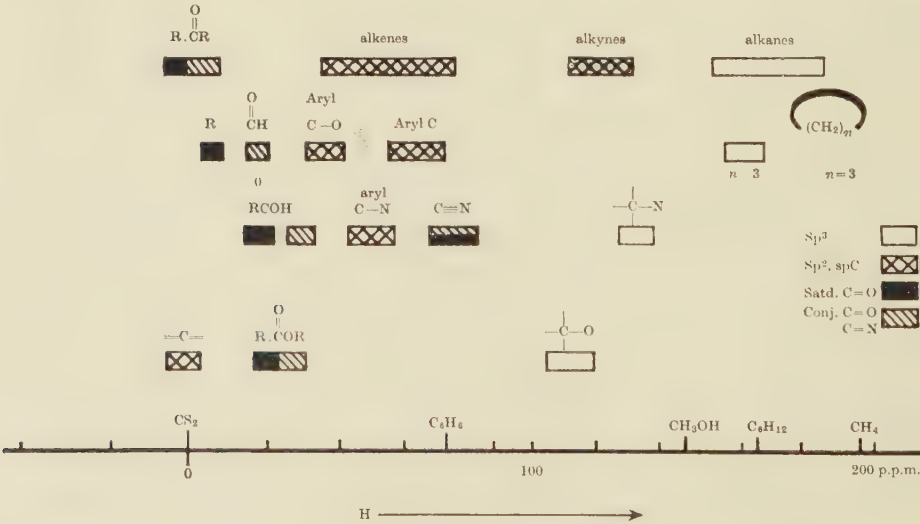
TABLE 35. Proton–Fluorine Spin Coupling Constants

	44–81
	7–13
	0
	1–8
	12–40
	o, 6–10 *m*, 5–6 *p*, 2

Refs.: (1) Banwell and Sheppard, *Disc. Faraday Soc.* **34**, 115 (1962); (2) Bernstein and Sheppard, *J. Chem. Phys.* **37**, 3012 (1962); (3) Banwell and Sheppard, *Mol. Phys.* **3**, 351 (1960); (4) Karplus, *J. Chem. Phys.* **30**, 11 (1959).

CORRELATION CHART II. ^{13}C Nuclei

The total variation in ^{13}C chemical shifts is at least 450 p.p.m. (*ca.* 7 kc/s at 15·1 Mc/s). The organic chemist has made little use of C^{13} n.m.r., but Lauterbur has pointed out that ^{13}C-labelled intermediates in biogenetic studies would aid the determination of the labelling pattern, as it could be obtained directly from ^{13}C spectra rather than degradative evidence. A correlation chart for ^{13}C chemical shift data is shown in Fig. 31.



A first-class review of the present knowledge of ^{13}C n.m.r. by Stothers is available to the interested reader. Other useful references are the following.

P. C. Lauterbur, *Ann. New York Acad. Sci.* **70**, 841 (1958).
J. B. Stothers, *Quart. Rev.* No. 2, 144 (1965).
^{13}C Studies. Acetophenones. K. S. Dhami and J. B. Stothers, *Can. J. Chem.* **43**, 479 (1965).
^{13}C Studies, Phenylketones. K. S. Dhami and J. B. Stothers, *Can J. Chem.* **43**, 498 (1965).
^{13}C Studies. Styrenes. K. S. Dhami and J. B. Stothers, *Can. J. Chem.* **43**, 510 (1965).

TABLE 36. ^{19}F Correlation Tables

The resonance frequency of the fluorine nucleus occurs at 37·65 Mc/s (9400 G). Line positions are very sensitive to solvent, thus causing difficulties in standardization A. G. Filipovich and J. V. D. Tiers, *J. Phys. Chem.* **63**, 761 (1959).

The chemical shift can be classified into a few groups according to the number of fluorine atoms bonded to the carbon atom; $—CH_2F$ appears at highest magnetic field, $—CF_2—$ next and $CF_3—$ lowest.

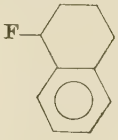
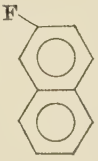
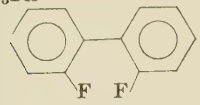
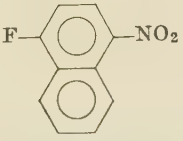
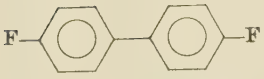
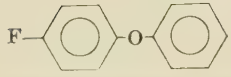
Compound	Shift p.p.m. from PhF as 0	Compound	Shift p.p.m. from PhF as 0
$nC_6H_{13}F$	102·8		10·2
CH_3FCOPh	117·1		
CH_2FPh	92·6		
$CH_2FCONHPh$	106·1		
$CH_2FCH_2CO_2H$	102·4		
$CH_2FCH_2CH_2OH$	106·0		
CH_2OH | $CH_2OCH_2CH_2F$	107·7		1·8
$PhCClF_2$	−63·8		
$CCl_2F—CCl_2F$	−46·6		
CF_3Ph	−49·9		
	1·5		−2·0
	2·6		
	7·0	$CF_3CONHPh$	−37·1
		$C_3H_7CONHPh$	−31·2, 7·2, 13·6

Table 37. Chemical Shifts of Phosphorus Compounds

The reference compound in these correlations is 85% aqueous phosphoric acid. Secondary standards are PBr_3 − 227 p.p.m., $(PhO)_3P$ − 127 p.p.m. and $(O—MeC_6H_4O)_3PO$ + 17 p.p.m.

GROUP SHIFTS FOR TRIVALENT PHOSPHORUS COMPOUNDS

Group	Br	Cl	I	OR	NR_2	OAr	F	S	Ar	R	H
Shift (p,p.m.)	−80	−74	−66	−55	−47	−42	−27	−23	0	+20	+69

Ref.: J. R. van Wazer, C. F. Collis, J. H. Shoolery and R. C. Jones, *J. Amer. Chem. Soc.* **78**, 5715 (1956).

Large deviations from these figures are possible and this is discussed in a review. R. A. Y. Jones and A. R. Katrizky, *Angewandte Chemie, Intern. edit.* 34 (1962), along with many other correlations.

Condensed phosphates and their derivatives δ p.p.m.

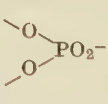
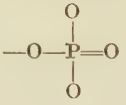
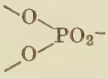
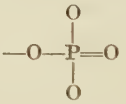
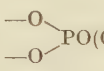
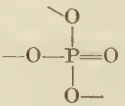
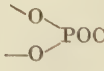
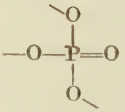
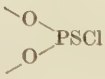
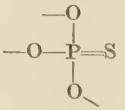
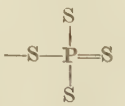
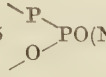
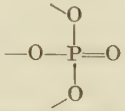
Isolated	δ	End	δ	Middle	δ	Branching	δ
PO_4^{3-}	−6	—O—PO_3^{2-}	+5				
HPO_4^{2-}	−3·5	—O—$PO_3H^{\ominus}$	+10				
$H_2PO_4^{\ominus}$	−0·5	—O—PO_3H_2	+10	In short chains	+18		
H_3PO_4	0			In rings or long chains	+20	Azeotropic Phosphoric acid	+34
$(EtO)_3PO$	+1	—O—$PO(Et)_2$	+13		+28		+41
$POCl_3$	−2	—O—$POCl_2$	+9		+30		+50
$PSCl_3$	−29	—O—$PSCl_2$	−28		−20		−3
		—S—$POCl_2$	−10				−60
$(Me_2N)_3PO$	−23	—O—$PO(NMe_2)_2$	−11.5		+12		+40

TABLE 37 (continued)

TRIVALENT PHOSPHORUS COMPOUNDS

Ligands			δ p.p.m.	Ligands			δ p.p.m.
CH_3	CH_3	CH_3	+61	F	F	F	− 97
Et	Et	Et	+20·4	Cl	Cl	Cl	−219
n-Bu	n-Bu	n-Bu	+32·3	Cl	Cl	Br	−225
Ph	Ph	Ph	+7	Cl	Br	Br	−228
Me	Me	$N(Me)_2$	−39	Br	Br	Br	−227
Me	Me	H	+98·5	I	I	I	−178
Et	F	F	+30	F	F	OMe	−111
Et	F	Cl	+20	Cl	Cl	OR	−181
Me	Cl	Cl	−191·2	OCH_3	OCH_3	OCH_3	−140
Ph	Cl	Cl	−162	OAr	OAr	OAr	−127
Et	F	iPrO—	−29	SR	SR	SR	−115·6
R	OR	OR	−183	NMe_2	NMe_2	NMe_2	−122
CH_3	SR	SR	−69·4	H	H	H	+240
CH_3	H	H	+163·5				

PHOSPHORYL COMPOUNDS

Ligands			δ p.p.m.	Ligands			δ p.p.m.
Et	Et	Et	−48·3	Cl	Cl	OH	−10
n-Bu	n-Bu	n-Bu	−43·2	Cl	OH	OH	−18
R	R	R	−46	OR	OR	OR	+5
CH_3	Cl	Cl	−44·5	OR	OAr	OAr	+17
Ph	Ph	Cl	−34	OR	OR′	OH	+0·5
R	OMe	OMe	−35	OAr	OAr	OAr	+17
R	OH	OH	−31.1	OH	OH	$O^{\ominus}$	0·5
R	SR	SR	−55·8	OH	$O^{\ominus}$	$O^{\ominus}$	−3·5
Ph	OH	H	−23	$O^{\ominus}$	$O^{\ominus}$	$O^{\ominus}$	−6·0
F	F	Cl	+15	SEt	SEt	SEt	−61·3
Cl	Cl	Cl	−3	NMe_2	NMe_2	NMe_2	−23·4
Br	Br	Br	+102				

THIOPHOSPHORYL COMPOUNDS

Ligands			δ p.p.m.	Ligands			δ p.p.m.
R	R	R	−51	Cl	Cl	Cl	−30
CH_3	Cl	Cl	−79·8	Br	Br	Br	+112
Ar	Cl	Cl	−74·8	Cl	OEt	OEt	−68·1
CH_3	OR	OR	−94·2	OMe	OMe	OMe	−73·0
CH_3	SR	SR	−74	OAr	OAr	OAr	−53
NR_2	NR_2	NR_2	−76·4	SEt	SEt	SEt	−92·9

Ref.: H. Finegold, *Ann. New York Acad. Sci.* **70**, 875 (1958); J. R. van Wazer, C. F. Collis, J. N. Shoolery and R. C. Jones, *J. Amer. Chem. Soc.* **78**, 5715 (1956); E. Fluck, J. R. van Wazer and L. C. D. Groenweghe, *J. Amer. Chem. Soc.* **81**, 6363 (1959).

The use of n.m.r. in the field of steroid chemistry has resulted in many correlations too vast to be included in this book, and the reader requiring such information is referred to the following list of references.

I.R., N.M.R. and U.V. of 900 Steroids "Steroid Spektrenatlas", W. Nendert and H. Röpke. Springer-Verlag, Berlin, New York.

Progesterones. E. J. Becker, R. M. Palmere, A. L. Cohen and P. A. Diassi, *J. Org. Chem.* **30**, 2169 (1965).

N.M.R. Studies on Steroids, VII, and papers sited therein. K. Tori and T. Komeno, *Tetrahedron* 309 (1965).

N.M.R. Spectra of some α-Halogenoketosteroids. C. W. Shoppee, T. E. Bellas, R. E. Lock and S. Sternhill, *J. Chem. Soc.* 2483 (1965).

N.M.R. of Acetoxy Protons in Steroids. J. N. Shoolery and M. T. Rogers, *J. Amer. Chem. Soc.* **80**, 5121 (1958).

N.M.R. Study of the Stereochemistry of some Steroidal 4,5-Epoxy Derivatives. *Tetrahedron Letters* No. 10, 623 (1963).

Conformation of Ring A in Steroids. *Tetrahedron Letters* No. 22, 1485 (1963).

Replacements Constant in Steroids. L. J. Leeson, J. E. Krueger and R. A. Nash, *Tetrahedron Letters* No. 18, 1155 (1963).

Steroidal sapogenins. W. E. Rosen *et al.*, *J. Amer. Chem. Soc.* **81**, 1687 (1959). J. P. Kutney, *Steroids* **2**, 225 (1963). J. P. Kutney *et al.*, *Tetrahedron* **20**, 1999 (1964).

The following lists a few references containing data of interest to the natural product chemist. Those marked * were used as sources for the correlation tables.

Compounds of the Limonine Type. D. L. Dreyer, *Tetrahedron* **21**, 75 (1965).

N.M.R. of some Polyenes. M. S. Barber, J. B. Davis, L. M. Jackman and B. C. L. Weedon, *J. Chem. Soc.* 2870 (1960).

An N.M.R. Study of Carbohydrates, 2,3-Epoxides and Related Compounds. D. H. Buss, L. Haugh, L. D. Hall and J. F. Manville, *Tetrahedron* **22**, 69 (1965).

*N.M.R. of Sugar Acetates. R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, *J. Amer. Chem. Soc.* **80**, 6098 (1958).

*N.M.R. of Phenols. R. J. Highet and P. F. Highet, *J. Org. Chem.* **30**, 902 (1965).

*N.M.R. of Methoxybenzenes. A. Zweig, J. E. Lehnsen, J. E. Lancaster and M. T. Neglia, *J. Amer. Chem. Soc.* **85**, 3940 (1963).

*N.M.R. of some Indoles. R. M. Acheson, *J. Chem. Soc.* 2631 (1965).

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1965, ix+179 pp.

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